LEARNING OF ACTION AND PERCEPTION IN WALKING

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A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy

Baltimore, MD
April, 2015

ABSTRACT

Motor adaptation is a trial and error process that allows us to adjust our movements in response to changes in our environment and our body. It is thought that this process recalibrates a forward model (potentially housed in the cerebellum), which predicts the sensory consequences of our motor actions. This has been typically thought to be a recalibration of the motor system. However, recent evidence in reaching adaptation studies has shown that there are also changes to sensory perception, specifically kinesthesia, that accompany motor changes. This dissertation examines which sensory perceptual changes occur during walking adaptation, the role of the cerebellum in these changes and how we can modulate them by changing the way individuals learn.

First, we studied changes in lower limb speed, position and force perception after subjects learned a new locomotor pattern on a split-belt treadmill. For each psychophysical experiment, we compared groups of healthy individuals who either learned a new pattern (experienced a 3:1 split-belt perturbation) or did not (walked at a tied fast speed). We found that of these three parameters, walking speed perception was the only one that changed significantly after learning a new walking pattern. We then went on to test whether this change to speed perception was a general one by testing generalization to a backwards walking direction. As expected, we found there was no transfer to the backwards direction in either the motor or speed perception domains. This suggests that the perceptual change may be specific to the context of walking and stem from the discrepancy between expected and actual leg motions following split-belt adaptation.

In our second study, we used the previous protocol for testing changes in speed perception in individuals with cerebellar ataxia. We compared this to healthy age-matched subjects. Surprisingly, we found that patients had preserved temporal components of motor adaptation, compared to healthy controls. We also found that in addition to spatial motor deficits, which we have previously shown, ataxia patients also showed aftereffect deficits in walking speed perception. These results implicate the involvement of the cerebellum in the recalibration of both motor and walking speed perception during split belt adaptation.

In our final study, we studied how we could modulate motor and speed perception aftereffects by changing the way subjects learned on the split-belt treadmill. We carried this out by applying different perturbations (abrupt versus gradual) to separate groups of healthy individuals. Surprisingly, we found that despite the fact that groups learned the same amount in the motor domain, the group that learned from a gradual perturbation showed much larger aftereffects in speed perception. This suggests involvement of another mechanism, perhaps one that deals with the explicit nature of errors, which can differentially affect the recalibration of sensory perception associated with learning a new walking pattern.

Taken together, these results suggest that walking speed is a salient perception that changes with split-belt adaptation, that it is affected by damage to the cerebellum and it can be changed depending on the size of errors experienced during learning.

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ACKNOWLEDGEMENTS

There are many people that have helped me in my lifetime and even before then to help me get to this point.

I would like to thank the undeniable support that I received from the teachers and professors that went out of their way to guide and encourage me. I would like to thank my advisor, Amy Bastian, for being an awesome mentor. She's helped me think like a rigorous scientist. Without an advisor like her, I may have quit long ago. Amy has shown me that work-life balance is important and achievable. I want to thank my other thesis committee members, Pablo Celnik and Reza Shadmehr for your insightful feedback and support throughout the years. I would also like to thank Allison Okamura, who previously co-mentored me along with Amy, for her contributions to my early graduate school work and for her support. Finally, I would also like to thank Larry Sass, one of my mentors from MIT, who guided and supported me along with many other students of color.

My graduate school experience would not have been the same without friends and labmates that have contributed to both academic and social aspects of my life. I want to thank everyone, old and new, from the Chibasnikowski group. Thank you to everyone that has contributed intellectually to my work. Special thanks to Matt Statton, a.k.a. "Stat Matt" whose feedback and editing have been critical for the publications we have started submitting based on the work in this dissertation. Thanks to everyone who has indulged in my entrepreneurial ideas during lunch conversations. Maybe one day, BTHT™ will become a reality. I have really appreciated the social atmosphere of the lab and it's been

important in getting through graduate school. I would like to thank my best friend, who's been a brother to me since high school, Nicolas Valentin, for supporting me throughout this journey. Nick has believed in me more than I have at times and I want to thank him deeply for that. I would also like to thank my oldest friends, Luis Mora, Fernando Escobedo and Mike Hansen for always believing in me. Also, special thanks to the Keswick Institute, which includes Jake Simson, Patrick Conlon and Sagar Shah for great times and for being great friends. Last but not least, I would like to thank Andrea Zamudio. Andrea, thank you for your support throughout this past year and for helping me open a new chapter in my life. Through you I have realized that, like in many facets of life, knowledge and skills can be used for good and for bad. Thank you for helping me to begin my journey to find my place in the struggle.

I would like to thank all of the subjects and patients that took time to volunteer in my studies. It was a pleasure interacting with patients and their families, which made all the hard work worthwhile. I would like to thank people who helped me with data collection and scheduling: Katie Amenabar, Rhul Marisigan and Joe Wang. Special thanks to my undergraduate mentee, Stefanie Busgang, who was invaluable help and sometimes went out of her way to do data collection and analysis.

My deepest gratitude goes to my family, blood and otherwise. My mom, Leticia, dad, Mario and brother, Elias, are the true champions who have created the most change within their means, more so than myself. They have stood resilient in the face of change and through extremely challenging moments. For you I have to thank for instilling in me the struggle, determination and humility through which I'm constantly realizing my goals and understanding my place in this world. To my mom, I want to thank you for being the

strongest person I know and for continuing to support every decision I make. To my dad, words can't express what your presence and hard work as a parent and role model have meant to me. To my brother, thank you for continuing to watch over me, guide me and for introducing me to the beauty of mathematics, science and music.

Finally, I want to thank my community as a whole, as my achievements are yours. The people before me that fought and risked their lives so I could be in this position today. I want to thank all of the beautiful people that are farmworkers, cooks, janitors, house maids, and many others that keep this country running. Know that my work is not any more important than yours and we are in this together. I hope that my accomplishments don't ever overshadow the systemic inequalities in our country. I want you to know that I will be conscious of how I use my talents as I move forward in life. Finally, I want to thank the ancestors before me, whose legacy in mathematics, science and medicine I continue.

DEDICATION

To Leticia, Mario and Elias.

LIST OF ABBREVIATIONS

$\Delta Force_{Post-Pre}$	$\Delta Force_{Post\_Test-Post\_Ref} - \Delta Force_{Pre\_Test-Pre\_Ref}$
ANOVA	Analysis of Variance
C	Control Group
CW	Clockwise
CCW	Counterclockwise
COD	Center of Oscillation Difference
CPG	Central Pattern Generator
deg	Degrees
Exp	Experiment
ICARS	International Cooperative Ataxia Rating Scale
LFTD	Left Fast Top Down Group
m	Meters
min	Minutes
Rev Group	Reverse Speed Task Group
RFBU	Right Fast Bottom Up Group
RFTD	Right Fast Top Down Group
s, sec	Seconds
SL_f	Fast Step Length
SL_s	Slow Step Length
Split Group	Split-Belt Adaptation Group

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CHAPTER 1

Background and INTRODUCTION

1.1 Overview of Sensorimotor Learning

All over the world people marvel at motor learning geniuses. Who are these people? Some of these people include athletes and musicians who are able to perform complex motor tasks with an extraordinary amount of precision and accuracy. These people complete many years of training to achieve this level performance and it is proof of the amazing capabilities and interplay between our brains and our bodies.

You are also a motor learning expert. OK, so maybe you can't fluidly play "Giant Steps" by John Coltrane or shoot free throws with a 90% success rate in the NBA, but you can constantly adjust and execute motor commands, coordinating over 600 muscles and hundreds of bones in your body. Seemingly ordinary tasks require the brain to orchestrate muscles, sense your body and environment and update movements when something does not go as planned. Moreover, our nervous system must deal with uncertainty in our environments as well as uncertainty in our movements, because after all, we are not perfect.

We tend to take our motor capabilities for granted and it is not until we undergo damage to our bodies or nervous system that we can appreciate them. Scientists and medical doctors study the roles of different parts of the brain by examining how damage to specific areas affects motor behavior. For example, a patient with cerebellar ataxia, with damage or degeneration of the cerebellum, will likely show general symptoms of incoordination and trouble with balance, gait, extremity and eye movements. This gives

us insight as to some of the behaviors that the cerebellum or a cerebellar-involved neural circuit is important for. Though sometimes it is hard to use a patient model to understand roles of brain regions in healthy people, because of the compensation that occurs by other regions, it is still a very useful model for researchers. Furthermore, it's important to study both healthy and patient populations to get a grasp of how humans learn and ultimately how we can help people with motor deficits regain proper control and move efficiently.

1.2 Overview of Motor Adaptation

As humans we constantly face unpredictable environments and situations in which we must act accordingly to accomplish our goals. The fact that we can instantly change our movements to adapt to such demands is proof of the amazing plasticity of our brains. Motor adaptation, which is usually thought of to take place on the order of minutes to hours, is a trial-and-error process we perform on a daily basis. Imagine, for example, you are playing a game of darts with some friends. Your goal is to try to hit the bull's-eye as close as possible. You aim for the center and perform your throw but you see the dart land to the left of the bull's-eye. You take this into account in your next throw by aiming more to the right than the previous one and you are able to get closer. Consider a different situation where you are riding a bike that has multiple gears. Let's say you are trying to achieve a constant speed. At a lower gear, you notice that applying a certain amount of force with each leg as you pedal produces a specific velocity and you have to adjust that force to achieve your desired speed. Then if you were to change gears, this relationship between force and your velocity changes and you will likely have to produce a different force to achieve the same speed. In both of these adaptation scenarios, your brain has information about the dynamics of the environment or object you are interacting with as

well as your own body. With every movement or "trial" your brain is making a prediction of the outcome of your movement and if it does not align with the actual outcome, it adapts your future movements to get closer to what you want to achieve.

In the laboratory, experimenters study motor adaptation in a controlled manner with a variety of motor tasks and equipment. Here I will briefly describe one of the most popular paradigms used and one that will be alluded to in this dissertation. In a visuomotor adaptation task, a subject will typically sit in front of either a tablet or robot and is asked to make reaching movements to various targets with a stylus or robotic manipulandum. They are given visual feedback of the location of their hand (which is unseen) as a cursor on a screen and try to get the cursor onto the target, starting from a home position closer to their body. During "baseline" subjects make reaches in which the cursor feedback is veridical, or is a true representation of their hand in space. Then during the "adaptation" period, a visual perturbation is introduced, sometimes abruptly and sometimes gradually, such that position of the cursor on the screen is shifted or rotated relative to the actual position of their hand. This initially causes large "end-point errors" in the direction of the perturbation. However, as subjects learn to compensate for the visual perturbation these errors are reduced closer to baseline levels. Finally, during the "post-adaptation" or "washout" period, the perturbation is removed and storage of the new visuomotor mapping learned is assessed. This learning is manifested as errors in the opposite direction of the perturbation, or "after-effects." This is actively unlearned and errors decay towards baseline values.

1.3 Locomotion and Adaptation

1.3.1 Background

Walking is a seemingly automatic process that allows us to navigate effortlessly from one terrain to another (e.g. from concrete to slippery ice). However, the complexity of the interactions between the nervous system and the body to achieve smooth gait is vast. Our nervous system must learn how to compensate on a short time scale (e.g. to avoid an obstacle on the sidewalk) as well as more persistent perturbations (e.g. learning to walk in high heels). Walking adaptation is inherently different than that of reaching adaptation because it is a continuous task and involves a different balance of afferent input (e.g. more proprioceptive than visual). Furthermore, the cost of error in walking may be higher than in reaching in that falling can be a very deleterious outcome.

1.3.2 Neural Control of Locomotion

Walking is an often highly stereotyped movement consisting of a sequence of muscle activations that allows for the transport of the body. One gait cycle begins with one heel contact of either foot and ends with heel contact of that same foot. One complete cycle is therefore comprised of two steps. One gait cycle is divided into two main phases: stance phase and swing phase. Stance phase can be further subdivided into four parts. Right stance phase begins with heel contact of the right foot and ends with toe-off of that same foot. During stance, the foot is on the ground and supports the body. The center of mass of the body moves forward over the foot and then the limb goes into extension. Right swing phase begins with right toe-off of the right foot and ends with heel contact of that same foot. Stance phase typically makes up about 60% of one gait cycle and swing phase about 40%. A right step length, as we define it in this work, is the anterior-

posterior distance between the right ankle at right heel contact and the left ankle at that moment and vice versa for the left step length. During locomotion, step lengths are typically symmetric and each leg is in anti-phase with the other such that when one leg is flexing the other is extending.

1.3.3 Spinal Circuitry in Locomotion

It was originally posed by Sherrington (Sherrington, 1910, 1914) that locomotion was the result of a chain of proprioceptive reflexes, the end of one movement phase of the step cycle triggering the beginning of the next. This was however, contradicted when it was observed by Graham Brown that locomotor-like rhythms could still be generated by the mammalian spinal cord after all sensory and descending input had been removed (Brown, 1911). This "intrinsic factor," as he called it, was able to produce the basic locomotor rhythm without descending control or sensory input. This later came to be known as the Central Pattern Generator or CPG (Grillner & Zangger, 1975). The behavior of CPGs isolated from sensory or descending inputs has been investigated and modeled in a variety of animals (Arshavsky et al., 1997; Grillner et al., 2000; Kiehn, 2006; McCrimmon et al., 2000; Rybak et al., 2006a; Rybak et al., 2006b; Selverston, 1993; Zelenin et al., 2000). The initial idea put forward was that each limb was controlled by a single CPG that consisted of flexor and extensor "half-centers" and coordinates with the CPGs of the other limbs (Cruse, 1990). However, it has since been suggested that individual joints are controlled by "unit CPGs" which are coupled to other CPGs (Grillner, 1981). It has been suggested that the isolated CPG is made up of an oscillator or "timing element" that creates the basic locomotor rhythm and an interneuronal network called the "pattern formation layer," which selects and modulates the activation

of single muscles (Lafreniere-Roula, 2005; Perret & Cabelguen, 1980; Perret, 1983). The most convincing evidence for the existence of CPGs comes from studies where afferent feedback is eliminated through blocking of movement. In such studies of "fictive locomotion," activity from efferent nerves are recorded at the ventral roots and have revealed rhythmic periods of activity that were reciprocally coordinated between agonists and antagonists (Marder & Bucher, 2001). While the existence of CPGs in humans is still debated, evidence for them comes from work in infants and patients with spinal cord injuries. Human infants, whose descending axons are not well myelinated and whose cortex are not fully mature, demonstrate stepping with specific spatiotemporal kinematics and muscle activation synergies (Altman & Bayer, 2002; Eyre et al., 2000) that are thought to be under spinal control (Yang et al., 1998). In patients with complete spinal cord injury, it has been shown that electrical stimulation of the lumbar spinal cord can induce step-like movements (Dimitrijevic et al., 1998).

1.3.4 Supraspinal Influences on Locomotion

In addition to influences from spinal circuitry and sensory inputs, animals must use information from other centers, above the spinal cord, to initiate locomotion, maintain balance and for the ability to adapt to new locomotor patterns. Some important structures include the brainstem, cerebral cortex and the cerebellum. The tracts that carry information from these brain regions that affect locomotion include the rubrospinal, corticospinal, reticulospinal, and vestibulospinal tracts. It has been shown that the mesencephalic locomotor region is important for initiating and controlling locomotion via projections to the reticulospinal nuclei (Armstrong, 1986). Cerebral cortex involvement in locomotion is less known but individuals with cerebral lesions/degeneration often

show abnormal gait impairments. One important involvement of the cerebral cortex that has been shown is in obstacle avoidance during locomotion (Drew, 1993; Drew et al., 2002). The cerebellum is a very important brain structure involved in modifying gait. Firstly, it receives sensory input from the limbs via the spinocerebellar tract as well as information from the spinal locomotor network via the ventral spinocerebellar tract (Arshavsky et al., 1978). It has also been shown that simple spike activity in the cerebellar Perkinje cells modulates with different parts of the gait cycle (Armstrong & Edgley, 1984). Furthermore, people with damage to their spinocerebellar tract often appear to have what is characterized as "drunken gait" (Serrao et al., 2012). Other structures may also influence locomotion to compensate for deficits. Recent evidence, for example, has shown that prefrontal cortex activity may be linked to gait compensatory mechanisms in cerebellar ataxia patients (Caliandro et al., 2015). Compensatory activation in the nervous system is important to consider when studying patient populations.

1.3.5 Split-belt Adaptation

For studying adaptation of walking patterns, a special split-belt treadmill paradigm can be used (Reisman et al., 2005). Like other adaptation paradigms, the idea is to put subjects in a novel situation and observe how they learn. The closest comparison for a real-world analogue of the split-belt is walking in a circle, as step lengths are asymmetrical. The split-belt treadmill has two belts that can be controlled independently and therefore can impose an asymmetric speed perturbation difference (usually 2:1 or 3:1) that subjects must learn to compensate for. In the case of split-belt adaptation, there are different kinematic parameters or errors that have been shown to adapt and retained

(Reisman et al., 2005) similar to end-point error in visuomotor adaptation. Split-belt protocols usually begin with a baseline period where the belts are tied and symmetric walking is assessed. Then the speed perturbation is introduced during adaptation and subjects learn how to make their initially asymmetric gait into a more smooth and symmetric one (within about 10 minutes). Then during post-adaptation, the belts are returned to tied and after-effects are similarly assessed as the new walking pattern is actively unlearned. It's been shown that both spatial and temporal parameters of gait can be adapted and are thought to be under independent control. They show different sensitivities to distraction, day-to–day consolidation and have different rates of development (Malone & Bastian, 2010; Vasudevan et al., 2011). The analysis of motor adaptation in this dissertation will focus primarily on step symmetry, which is a parameter involving step lengths and can be changed via both spatial and temporal parameters. In Chapter 3, we will include further analysis with more specific spatial and temporal parameters.

1.4 Sensory Control of Movement

1.4.1 Background

In order to move about in any environment, animals need a variety of sensors to give them information about their movements and the things around them. Reflecting this, a particular saying goes "we cannot control what we cannot sense." In order to understand how the nervous system updates movements accordingly we must begin by examining the different sensory receptors and circuitry necessary that ensure our bodies are carrying out a correct motor behavior. Some of these senses are more important than others for certain types of motor behavior. This section we will focus on kinesthesia, or

the ability to sense limb position and movement. The term proprioception will also be used in this dissertation, which is typically used to indicate sense of limb position.

1.4.2 Kinesthetic Receptors

We are often confronted with situations where we cannot rely on our sense of vision to complete a task. For example, consider looking for your keys in a dark room or in your bag. In these situations we primarily rely on our kinesthetic sense, a more mysterious sense that allows us to estimate the position and movement of our limbs as well as amount of force exerted or acted on us. We have various types of receptors, each coding for different kinesthetic parameters, which provide information to our central nervous system. It's important to note that the receptor population response as a whole is ultimately used to generate this information and not simply single receptor responses. Furthermore, the receptor information can be used differently when a person is moving voluntarily in an "active" task versus a "passive" state where no motor commands are being executed.

Kinesthesia has been shown largely to be mediated by muscle spindles (Goodwin et al., 1972; Ribot-Ciscar et al., 2003) as well as skin stretch receptors (Collins et al., 2005). Muscle spindles can respond to muscle length change (position) and rate of length change (speed) (Matthews, 1972). For skin receptors, it is thought that slowly adapting type II receptors signal position (Chambers et al., 1972; Edin, 1992; Edin, 2004). Particularly in the lower-limbs, there is also evidence that shows that receptors in the hairy skin (SA III) can provide high-fidelity information about knee joint movements (Edin, 2001). Although once thought to be a primary receptor for measuring limb position, joint receptors have a limited role (Burke et al., 1979; Proske & Gandevia, 2009) as they signal

position at extremes, serving as limit detectors. When an object is pressed against one's body, with the body in a static state, it is thought that the main receptor for encoding this force is mechanoreceptors in the skin (Purves, 2008). However, during an active push against an object, it is thought Golgi tendon organs (GTO) (Ib afferents), located between muscles and tendons play a primary role in signaling the tension in a muscle (Purves, 2008). It has also been recently shown that that Ib afferents also contribute to the sensing of joint velocity in a hand grasp study, where primary and secondary afferent firing rates were well correlated with joint velocity but not with position (Dimitriou & Edin, 2008).

1.4.3 Sensory Control of Locomotion

It has been shown through neuromechanical simulations that sensory input is crucial to maintaining stable stepping in addition to output from timing and pattern formation elements of locomotor CPGs (Ekeberg & Pearson, 2005; Pearson et al., 2006; Taga et al., 1991; Taga, 1995; Yakovenko et al., 2005). Though cutaneous receptors contribute to kinesthesia they are to a lesser degree important for locomotion. They only fire at discrete times in the step cycle, for instance, upon ground contact (Loeb, 1981). They have polysynaptic reflex actions on α-motoneurons and may influence the timing of locomotor phase transitions (Rossignol et al., 2006) and can trigger a stumble corrective reaction (Forssberg, 1979; Haridas et al., 2008). Muscle spindles and GTOs however, seem to be involved more in the continuous reflex control of α-motoneurons and the timing elements of the locomotor CPG during stepping as they fire continuously throughout the step cycle (Geyer et al., 2003; Grey et al., 2007; Prochazka et al., 1997; Shemmell et al., 2010). In addition to reflex control, it has been seen that sensory input can trigger step cycle phase transitions. In particular, GTOs have been shown to be

important in this signaling, activating extension and flexion in the legs appropriately for rhythmic locomotion (Duysens et al., 2000). Another possibility for the role of sensory input in the gait cycle is to vary phase duration. This has been shown by artificially stimulating tendon organ afferents that normally signal extensor force, which results in a delay in the stance-to-swing transition (Pearson, 2008). Similarly, stimulating hip muscle afferents that signal hip extension delays the transition from swing to stance (Hiebert et al., 1996).

1.5 Sensorimotor Recalibration

1.5.1 Sensory weighting and realignment

Sometimes different senses give our brain information that is in disagreement. Consider the situation of picking up a coin from a fountain. As you reach your hand through the water, you see a "ghost image" of your hand due to the refraction of light. This causes a mismatch between what you see (visual feedback) and what you feel (kinesthetic feedback). Initially this can create an error and failure to make an accurate movement towards the coin. It is thought that there are two distinct ways the brain can resolve this mismatch. On one hand, it is possible to employ a realignment strategy where the spatial relationship between the sensory estimates is changed such that for example, the proprioceptive estimate of hand position realigns to more closely match the visual estimate, vice versa (Block & Bastian, 2011; Van Beers et al., 2002) or it is possible they both change. After the realignment occurs, the brain integrates these new estimates to calculate one unified estimate. The benefit to this strategy is that information from both is still preserved and the integrated estimate also has a smaller variance than the unimodal estimates (Ghahramani et al., 1997; Maybeck, 1979). On the other hand, another strategy

which has been studied extensively is reweighting (Ghahramani et al., 1997; van Beers et al., 1999). In this strategy, the visual and proprioceptive estimates are each given a certain weight and then are appropriately integrated to create a unified estimate of hand position. Interestingly, it does not appear that realignment is dependent on reweighting but rather that they are processes that are controlled independently, and either can be used to compensate for a sensory misalignment (Block & Bastian, 2011).

In the example of reaching into a fountain, the reweighting or realignment of the sensory inputs can occur concurrently with motor adaptation because of the sensorimotor error that is observed at the end of the reach (e.g. how far off you were from the coin). Can sensory realignment occur independently of motor adaptation? Block and Bastian (2012) investigated this question by testing cerebellar ataxia patients and healthy subjects in a realignment task. Cerebellar patients are known to have motor adaptation deficits and this was confirmed by the study. Interestingly, they showed that during a reaching task where a gradual visuo-proprioceptive error is introduced, if visual endpoint feedback (i.e. error that drives motor adaptation) is removed, the patients could realign their proprioceptive and visual sensory estimates as well as controls. These results suggest that motor adaptation is not necessary for sensory realignment and that the cerebellum is not critical for this particular type of realignment to occur. However, it may be that analogous kinesthetic estimates change differently in walking adaptation.

1.5.2 Perceived Sensory Changes Concurrent with Motor Adaptation

1.5.2.1 Reaching

Several studies have shown a phenomenon in which sensory perception changes alongside motor adaptation. These studies have almost exclusively focused on sense of

hand position and reaching. In this body of work, experimenters use one of two main reaching adaptation paradigms: visuomotor or force-field adaptation. In the more popularly used visuomotor paradigm, subjects must make reaches to targets using a stylus on a tablet or a robotic manipulandum while receiving altered visual feedback of their hand position. This creates a sensory mismatch between what subjects see and what they feel. In order to achieve the task goal, which is to move their hand representation (cursor) through the target, subjects must learn a new visuomotor mapping. For example, if a cursor is rotated in the clockwise (CW) direction, relative to the trajectory of their arm, subjects must compensate by aiming in the counter-clockwise (CCW) direction to move the cursor onto the target. Motor learning in this case is usually assessed by measuring the end-point reaching error, which is the angle between the line connecting the start point and target and the line connecting the start point and the position achieved at the end of the movement. The minimization of this error and "after-effects" in the opposite direction, when the perturbation is removed, demonstrates motor adaptation and retention. Importantly, in addition to motor adaptation, these paradigms assess subjects' estimates of hand position before and after learning this new visuomotor map. This is typically achieved by carrying out a standard 2-alternative forced choice task where subjects are asked whether they feel their hand position to be to the left or right of a reference marker. These studies have shown that after adapting to the visual perturbation, their sense of hand position is shifted such that it is more in line with the visual feedback they received. For example, if before adapting to a 30 degree CW (positive) perturbation, they felt their hand to be at zero degrees (in front of the body), after adaptation they would feel it to be shifted in the CCW (negative) direction (e.g. -6 degrees).

From reaching studies, it is unclear as to how learning in the motor domain is related to changes in sensed hand position and whether one process underlies the other. To investigate this relationship studies have tried to correlate the magnitude of change in motor performance in a visuomotor adaptation task with the amount of change in perceived hand position. On the one hand, some studies (Cressman & Henriques, 2009; Salomonczyk et al., 2011) have not shown any significant correlation between these two parameters while Ostry et al. (2010) showed a significant correlation. Other (Cressman & Henriques, 2010a; Salomonczyk et al., 2013) studies have shown that when subjects experienced a cross-sensory error, where they did not produce voluntary movements but experienced a visual/proprioceptive mismatch, they could still induce a change in felt hand position as well as small motor aftereffects. These mixed results further warrant the need to investigate the relationship between motor adaptation and perceptual changes.

1.5.2.2 Walking

In walking, only one study, to our knowledge (Jensen et al., 1998), has shown perceptual aftereffects following the experience of a perturbation. This study showed if healthy subjects experienced a 3:1 split-belt perturbation, such that one leg was controlled to move three times as fast as the other, subjects experienced perceptual speed aftereffects such that the "slow" leg during adaptation felt faster afterward and the fast leg felt slower. The aim of this study was not however, to relate these perceptual changes to motor behavior and therefore, there were no kinematic data collected. The main focus of this dissertation is to further explore this phenomenon and to investigate its relationship to motor learning, the cerebellum and how we can modulate it.

1.6 Cerebellum in Motor Adaptation and Sensory Perception

1.6.1 Background

As alluded to previously, the cerebellum is an important brain structure that is located posterior to the brainstem and inferior to the occipital lobe. It is important for executing coordinated, accurate and precise movements and for maintaining flexibility in motor behavior. It does not initiate movement by itself but rather does so in conjunction with other motor areas of the cerebral cortex (Purves, 2008). It has also been speculated to have a possible role in sensory processing (Gao et al., 1996; Hagura et al., 2009; Parsons et al., 1997). For this reason, it is a prime target of investigation for understanding the potential links between motor and sensory perception recalibration.

1.6.2 Cerebellar Ataxia

Damage or degeneration of the cerebellum is clinically diagnosed as ataxia, which means "without coordination." Although ataxia patients typically have normal strength they make inaccurate, jerky and variable movements (Holmes, 1917). When prompted to reach to a target, patients tend to over- or undershoot (Hore & Flament, 1988; Manto et al., 1994; Trouillas et al., 1997). Ataxic walking is typically characterized as 'drunken gait' that is marked with uncertain starts and stops, lateral deviations and asymmetric steps (Serrao et al., 2012). A standard clinical rating scale that looks for a variety of these symptoms is the International Cooperative Ataxia Rating Scale (ICARS; Trouillas et al., 1997). The scale involves a compartmentalized quantification of postural and stance disorders, limb ataxia, dysarthria and oculomotor disorders. In this dissertation, we use the ICARS to rate our ataxia patients and use the gait and posture subscore to gauge severity.

1.6.3 Cerebellar internal models

It is still unclear exactly which computations the cerebellum calculates to affect movement and sensory processing. Some theories that have been proposed include the cerebellum as a processor of time (Hore et al., 1991; Ivry & Spencer, 2004), muscle activation scaling (Holmes, 1917; Manto et al., 1994), interaction torques (Bastian et al., 1996; Bastian et al., 2000), predicted versus actual movement (Allen & Tsukahara, 1974) and sensory information and discrimination (Gao et al., 1996).

One popular theory that uses various aspects of those detailed above is that the cerebellum is important for updating and/or storing internal models (Wolpert et al., 1998; Kawato, 1999) that are used for movement and perception. Internal models simulate the response of the motor system in order to estimate the outcome of a motor command. There are two primary types of internal models: inverse models and forward models. A potential inverse model in the cerebellum would generate the sequence of motor commands that take into account the dynamics of the body (Gomi & Kawato, 1992; Kawato & Gomi, 1992a, 1992b). On the other hand, a forward model would predict the sensory consequences of action (Doya, 1999; Izawa & Shadmehr, 2011; Miall & Wolpert, 1996; Paulin, 2005; Shadmehr & Krakauer, 2008) and then compare predictions to actual sensory feedback to update future movements. It is thought that forward models predict sensory consequences of movement to compensate for time-delayed sensory feedback (Miall et al., 1993) and could also control proprioception during movement (Wolpert et al., 1995). It has also been suggested that the cerebellum may use both types of internal models (Wolpert et al., 1998).

1.6.4 Cerebellum and Motor Adaptation

It has been shown in a variety of paradigms that humans and other animals with cerebellar damage have difficulty adapting their movements in response to perturbations. This has been shown in reaching paradigms (Criscimagna-Hemminger et al., 2010; Donchin et al., 2012; Maschke et al., 2004; Rabe et al., 2009; Smith & Shadmehr, 2005; Taig et al., 2012; Werner et al., 2010; Werner et al., 2009), prism adaptation (Baizer et al., 1999; Fernandez-Ruiz et al., 2007; Martin et al., 1996a, 1996b) and split-belt walking adaptation (Morton & Bastian, 2006). This evidence argues for the cerebellum being involved in the prediction or accurate estimation of consequences of motor commands. Though still under debate, studies have shown that given gradual perturbations that result in smaller sensorimotor errors, patients can adapt and retain learned reaching motor behavior (Criscimagna-Hemminger et al., 2010; Henriques et al., 2014; Izawa et al., 2012). However, other work has shown that there may still be a deficit with both abrupt and gradual perturbations (Gibo et al., 2013; Schlerf et al., 2013). The conflicting evidence again warrants further investigation of motor learning in cerebellar patients, especially in walking, where much less research has been conducted.

1.6.5 Cerebellum and Sensory Perception

Sensory perception involves combining various sensory modalities (sight, sound, touch, smell, taste) and integrating them into something coherent so that we can have meaningful experiences. Different types of sensory information are processed in different parts of the brain before ultimately coming to the level of perception. Posterior parietal cortex has been implicated to be an important part of the brain that integrates different sensory modalities (Stein & Stanford, 2008).

Early studies of the cerebellum proposed it to have a small role in sensory processing (Dow & Moruzzi, 1958; Holmes, 1917). However, more recent neuroimaging studies have shown significant activity in the cerebellum during visual and auditory perceptual tasks (Baumann & Mattingley, 2010) as well as somatosensory processing tasks (Gao et al., 1996). More recent work has also shown that the cerebellum is important for active force perception (Bhanpuri et al., 2012). Directly relevant to this dissertation, is work that has tried to elucidate the cerebellum's involvement in changes in hand position perception after experiencing visuomotor perturbations in reaching. On one hand, some studies (Izawa et al., 2012; Synofzik et al., 2008) have shown that damage to the cerebellum produces deficits in changes to hand position perception, such that healthy controls recalibrate their sense of hand position after visuomotor adaptation but patients do not. On the other hand, another study (Henriques et al., 2014) has shown, that cerebellar ataxia patients can both adapt and learn from a gradual visuomotor perturbation as well as show perceptual kinesthetic aftereffects, similar to healthy controls. From these results, Henriques and colleagues implicate that the cerebellum is not necessary for visually driven recalibration of hand proprioception. As it is uncertain from conflicting results and the difference in reaching versus walking adaptation, it is important to test analogous perceptual changes in patients learning a new walking pattern. This allows for gaining a better understanding of the role of the cerebellum in perception for a different task/set of effectors.

1.7 Error Size and Sensorimotor Learning

1.7.1 Background

Imagine you just bought a new pair of prescription glasses and you try them on for

the first time. When you put them on and look at your hand as you reach for an object, you might notice something off with where you expect your hand to be and its actual position. This is due to the shifting of your visual field; since it's only a slight visual perturbation you are able to compensate very quickly and move about your day. Now imagine that you put on a weird pair of glasses that completely shifts your visual field, such as with a prism adaptation paradigm (Martin et al., 1996a, 1996b). Now what you might find is that this large abrupt visual perturbation is causing much larger errors as you reach for an object and this will take longer to adapt to before you can make accurate movements. In the laboratory, researchers have studied the difference between perturbations that are large and abrupt (e.g. prism glasses) and gradual incremental ones (e.g. regular eye glasses). These are important because they give us insight on how the nervous system is able to compensate for these errors during adaptive learning as well as how they are interpreted and how learned behavior is retained in these different cases. Furthermore, there are clinical implications for this type of work in that different learning environments may make it easier for patients with sensorimotor deficits to learn and retain new behavior.

1.7.2 Credit Assignment

The idea of credit assignment is important to understand how different magnitudes of errors affects how one learns, retains new behavior and generalizes to other situations. Credit assignment is the ability to assign errors to the environment or the body. If on the one hand, the source of error that drives learning is designated to be the environment, one would ideally adapt and apply learning to that specific situation or context. However, if the source of error is assigned to be the body, through one's own faulty movement, then

one is more likely to apply the learning to other movements. With this rationale, it is clear how experiencing a large abrupt error might lend itself to assignment of error to the environment. For example, on the split-belt treadmill it would be clear if one leg is driven three times as fast as the other, that this would be perceived as unnatural and therefore errors should be attributed to the treadmill. However, if the belts were split gradually without explicitly telling a subject, they would be more likely to attribute any errors to their own doing.

1.7.3 Motor Adaptation and Error Size

In line with the idea of credit assignment, it's been shown that the history of errors experienced during learning can affect how much one learns and how that learning transfers to different situations. Previous studies have showed that the size of errors (Körding & Wolpert, 2004; Wei & Körding, 2009) and their variability during learning can affect the rate of learning (Burge et al., 2008; Korenberg & Ghahramani, 2002; Wei & Körding, 2010) or what we learn. In terms of retention, it is thought that learning from a gradual perturbation results in a more stable motor memory (Huang & Shadmehr, 2009). Studies of reaching adaptation have shown that gradual perturbations can lead to larger motor aftereffects immediately after learning (Kagerer et al., 1997) and greater retention 24 hours later (Klassen et al., 2005) compared to abrupt perturbations. Gradual perturbations can also lead to more robust generalization when the trained arm is used in a different context (e.g. unconstrained reaching) when compared to abrupt perturbations (Kluzik et al., 2008). Similarly, in split-belt treadmill walking adaptation, it has been shown that imposing errors throughout adaptation that are more natural, can produce larger transfer to overground walking than unnatural errors (Torres-Oviedo & Bastian,

2012).

1.7.4 The Cerebellum and Error Size

There is evidence that the learning and retention of motor memories from small versus large errors might engage different neural structures or mechanisms of plasticity. In particular, related studies on the cerebellum have revealed such distinctions. One study in monkeys showed that inactivation of the cerebellar dentate nucleus created deficits in gradual but not abrupt adaptation (Robertson & Miall, 1999). In another study, Boyden and colleagues (2006) studied motor retention in knockout mice whose maintenance of long-term depression (LTD) in parallel fiber-Perkinje cell synapses in the cerebellum was disrupted. They found that disruption of LTD maintenance in the cerebellar cortex affected retention of memories acquired through experiencing large errors but not small errors. Supporting this evidence, reaching adaptation studies in patients with cerebellar damage have shown that they are able to adapt and retain motor memories when learning from gradual force, or visuomotor perturbations (Criscimagna-Hemminger et al., 2010; Henriques et al., 2014; Izawa et al., 2012).

1.7.5 Perceptual Recalibration and Error Size

Within the framework of credit assignment, one might expect that in addition to larger motor retention with a gradual perturbation, that the phenomenon of perceptual recalibration might also produce larger after effects when learning from small errors. There have not been, to our knowledge, studies *explicitly* comparing the perceptual aftereffects of abrupt versus gradual perturbations. Different studies have reported recalibration of felt hand position after both learning from abrupt (Cressman & Henriques, 2009; Haith et al., 2008; Ostry et al., 2010) and gradual (Salomonczyk et al.,

2011; Salomonczyk et al., 2012) visuomotor and force field perturbations. One recent study (Mattar et al., 2013) however did show a trend toward larger perceptual aftereffects for a force-field perturbation that was introduced gradually versus abruptly but this result was only anecdotal as conditions were not compared explicitly. In Chapter 4 of this dissertation, we discuss how perceptual aftereffects are differentially affected by learning from small versus large errors.

SCOPE OF THIS DISSERTATION

This dissertation aims to understand changes in perception that accompany split-belt walking adaptation in both healthy and cerebellar ataxia patients. We developed psychophysical tasks that measure lower-limb position, speed and active stepping force. Unlike analogous reaching adaptation studies that find changes in position perception, we found robust changes only in speed perception that occurred with motor learning. We then used the same speed perception paradigm to investigate whether damage to the cerebellum affects both motor and perceptual recalibration. Finally, we investigated how we could modulate speed perception recalibration by changing the type of perturbation imposed on healthy subjects. Our findings improve the current knowledge of both motor learning as well as the limited understanding of lower-limb perceptual recalibration and how the two are related. Clear cerebellar patient deficits in recalibration of speed perception lend to the possibility of using our speed task paradigm as another clinical test to probe for cerebellar damage. Much of the work presented here has been presented in the form of abstracts. Chapter 2 is very closely related to a publication currently under review and Chapters 3-4 are modifications of manuscripts, which are currently under preparation.

In Chapter 2, we used 3 perceptual tasks we've developed to investigate changes in perceived leg speed, foot position and stepping force after learning a new walking pattern. The perceptual tasks were completed before and after walking with either split-belts (error-based learning) or fast-tied belts (non-learning), depending on which group subjects were randomly assigned to. Our walking speed perception task consisted of subjects attempting to match one leg's speed to match their other leg speed, which was

held constant. They carried out the task by using a keypad to incrementally change the speed of one leg to match the other. To quantify the decay of this recalibration, we had subjects conduct the task at six time points during the post-adaptation period. The position task was done by having the treadmill move one of the legs to different pre-defined locations either in front or behind the other reference leg. Subjects verbally responded whether they felt the moved leg was in front or behind the other. Finally, in our active stepping task, subjects used visual feedback on a display to step down with different magnitudes of forces (relative to body weight) and recreate the same force with no visual feedback with the other leg. Interestingly, we found significant pre/post-adaptation changes in speed perception only. We were able to confirm results from a previous study, quantify the post-adaptation perceptual decay, as well as add the motor recalibration results that accompanied these changes. Additionally, we investigated how generalizable this speed recalibration phenomenon is by having a separate group of subjects learn forward walking adaptation and then carry out the task with backwards walking. As we expected, no transfer occurred either in the motor domain (confirming previous results) or perceptual domain, suggesting this effect is specific to the learned direction/context and is not a general speed recalibration. Overall, our findings are fundamental in understanding perceptual changes in the lower-limbs due to motor learning, exploring perceptual parameters reaching studies have yet to investigate.

In Chapter 3, we used our speed matching task paradigm from Chapter 2 to try to understand the role of the cerebellum (which holds a putative forward model) in the leg speed recalibration phenomenon and whether it is tied to any specific components of motor adaptation. We used a cerebellar patient model to carry out this study, testing

patients with cerebellar ataxia and age-matched controls. As in Chapter 2, subjects carried out the task before split-belt adaptation and at six time points after adaptation. We found that patients do not recalibrate their sense of leg speed after an abrupt split-belt perturbation (2:1 ratio) was imposed on them, while controls showed similar robust aftereffects to the healthy young subjects in Chapter 2. We were also interested in understanding how motor adaptation played a role in these perceptual deficits. In previous studies, we've shown that spatial and temporal components can be adapted independently and that cerebellar patients may have more preserved timing, which may be more reliant on other structures, intact in cerebellar patients. We therefore split our motor adaptation analysis into spatial and temporal components. Our results showed for the first time that cerebellar patients may be able to learn as much as healthy controls in the temporal domain but have marked deficits in spatial components. Further analysis showed that all subjects, patients and controls, appeared to be recalling spatial components of learning when trying to achieve perceptual symmetry in the post-adaptation speed tasks. We also found a relationship between the amount of learning in a spatial motor component and the amount of recalibration in the perceptual speed domain. Taken together, these results give us more insight on how subjects achieve perceived inter-limb speed symmetry and on specific motor and perceptual deficits of cerebellar patients. We interpret these findings as more evidence that suggests the cerebellum holds a forward model that predicts the sensory consequences of movement. Furthermore, the clear perceptual deficits in patients may allow for the use of our speed-matching task as another clinical test, which can provide therapists and researchers with further evidence of potential cerebellar damage.

In Chapter 4, our investigation turned back to healthy young individuals and asked whether we could modulate the amount of motor and speed perception aftereffects by changing the environment in which subjects learned. Previous studies have shown that when a perturbation is imposed gradually (small errors) rather than abruptly (large errors), retention of learned motor behavior may be increased. Other studies have also showed increasing the length of adaptation may increase retention. As such, we investigated how abrupt and gradual perturbations changed motor and perception aftereffects. We modified our previous speed matching paradigm such that subjects completed the post-adaptation task over the course of 15 minutes rather than multiple short tasks. This allowed us to observe how the perceptual aftereffects decayed, if at all, when subjects were constantly trying to achieve perceived speed symmetry. Our results surprisingly showed that the 3 groups (Gradual, Abrupt and Extended Abrupt) learned equivalently in the motor domain. In a separate group of subjects that experienced the same perturbations, we found that the Gradual group exhibited significantly larger speed perception aftereffects, again despite showing similar motor adaptation. Our results suggest that there may be some implicit component of motor adaptation in the Gradual group that preferentially recalibrates perception, different to that of the Abrupt groups. These results are the first to directly compare abrupt versus gradual perturbations within the context of perceptual recalibration and motor learning. Our findings are important for re-thinking how we conventionally measure sensorimotor adaptation.

In Chapter 5, the important results of this dissertation are summarized and potential future directions along with clinical implications are outlined. This work provides fundamental psychophysical findings that have yet to be explored in the context of the

lower limbs and walking adaptation.

CHAPTER 2

Perceptual Sensory Correlates of Split-Belt Adaptation

2.1 Introduction

Recent work has shown that reaching adaptation not only recalibrates the motor system, but can also result in changes in kinesthesia (the sense of limb position and movement). Studies in healthy adults have shown that perceived hand position can change after adapting to a force field perturbation (Haith et al., 2008; Ostry et al., 2010; Mattar et al., 2013), a visuomotor rotation (Cressman and Henriques, 2009; Salomonczyk et al., 2011; Salomonczyk et al., 2012) and after experiencing discrepancies in visual and proprioceptive estimates of the hand (Cressman and Henriques, 2010a; Salomonczyk et al., 2013). One idea is that changes in kinesthesia are a result of recalibration of a forward model that predicts the sensory consequences of movement (Izawa et al., 2012). For example, Cressman and Henriques (2009) showed that a visuomotor perturbation to reaching movements resulted in a roughly 20% change in perceived hand position relative to the magnitude of both a translation perturbation and a rotation perturbation. This motor and sensory recalibration appears to rely on intact cerebellar function (Synofzik et al., 2008; Izawa et al., 2012). This suggests that changes in the perception of hand position are a result of an error-based adaptation in the motor domain.

Yet, other studies suggest that these types of perceptual changes can represent a process that is independent from adaptation and forward model recalibration. One recent

example from Cressman and Henriques (2010a) showed that people have aftereffects in both motor and perceptual domains after subjects were exposed to a sensory mismatch in the absence of movement related error signals. Another is the well known "rubber hand illusion" in which proprioceptive sense of the arm can be biased following synchronous tactile stimulus of a subjects unseen hand and a displaced rubber hand that the subject can see (Botvinick & Cohen, 1998). Finally, we have shown that patients with cerebellar ataxia can change their proprioceptive hand estimates to match a visual estimate, independent of motor adaptation (Block & Bastian, 2012). These results suggest that although motor and sensory recalibration processes often take place simultaneously, motor adaptation is not necessary for sensory realignment to occur.

To date, most work has focused on adaptation of movements of the arm. It is well known that similar motor adaptation processes occur during walking. We have previously shown that split-belt treadmill walking adaptation leads to adaptation and storage of several kinematic measures including step length and timing (Reisman et al., 2005; Morton & Bastian, 2006; Choi & Bastian, 2007; Choi et al., 2009; Vasudevan et al., 2011; Malone & Bastian 2010; Malone et al., 2012) and kinetic parameters such as ground reaction forces and the center of pressure (Mawase et al., 2013). It is unclear whether perceptual changes will also occur in any of these domains. Walking and reaching are also controlled by different neural circuits, though both involve the cerebellum. Therefore, they both might show similar effects from recalibration of a forward model.

Little is known about changes in the perceptual-kinesthetic domain during walking. We are only aware of one study that investigated changes in speed perception

after split-belt walking. Jensen and colleagues (1998) found that after split-belt walking, subjects experienced a perceptual aftereffect such that the leg that experienced a fast speed felt slower afterward and vice versa. In that study, kinematic data was not recorded, so investigators could not examine the extent of motor learning or the relationship between motor and sensory aftereffects of learning. Furthermore, changes in other perceptual parameters such as position and force have not been investigated in the context of split-belt adaptation. Here we asked which perceptual sensory changes, if any, are associated with split-belt adaptation and how they relate to changes in the motor domain. The study was divided into separate experiments to independently measure perception of leg speed, foot position, and stepping force. We hypothesized that split-belt adaptation could lead to perceptual changes in all three parameters.

2.2 Materials and Methods

2.2.1 Subjects

Ninety right hand and right leg dominant volunteers (38 M, 52 F; Age: 23 yrs ± 3.3) participated in this study. All subjects were prescreened for self-reported handedness and neurological/motor dysfunction. The protocol was approved by the Johns Hopkins Institutional Review Board and all participants provided written informed consent before testing.

2.2.2 Experimental Setup

Split-belt treadmill. Split-belt walking adaptation was studied using a custom-built treadmill (Woodway, Waukesha, WI) which had two separate belts driven by independent motors. Speed commands for each belt were sent to the treadmill through

either a custom MATLAB (The MathWorks, Natick, MA) program or a custom Python program in the Vizard (WorldViz, California USA) development environment, depending on the task performed by the subject. Vertical forces exerted on each belt were recorded at 1000 Hz. Subjects wore a safety harness which did not support their body weight and were positioned in the middle of the treadmill with one leg on each belt.

Optotrak Motion Analysis. Kinematic data were collected at 100 Hz using Optotrak (Northern Digital, Waterloo, ON, Canada). Bilateral infrared-emitting markers were placed over the toe (fifth metatarsal head), ankle (lateral malleolus), knee (lateral femoral epicondyle), hip (greater trochanter), pelvis (iliac crest), and shoulder (acromion process)

Perceptual Tasks. We studied sensorimotor perception of walking speed, leg position, and stepping force before and after walking in different conditions. This was done using custom Python programs to control the treadmill, provide real-time visual feedback, and collect subject data.

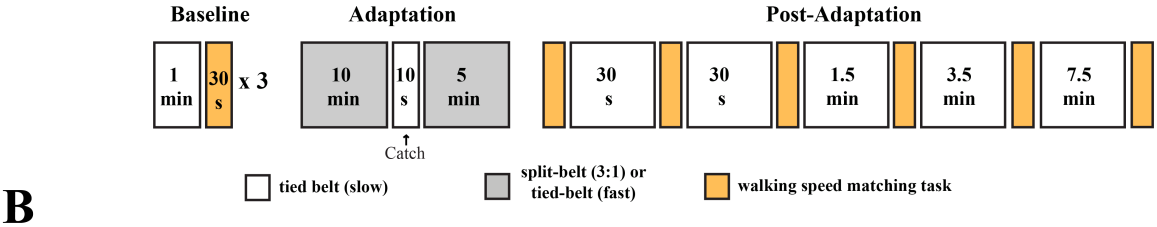
2.2.3 Experimental Protocols

2.2.3.1 Split-Belt Walking Adaptation

In all experiments, the split-belt walking paradigm consisted of four main walking periods (Figure 2.1A), as follows: Baseline: all subjects walked with tied belts (.5 m/s). Adaptation: subjects experienced either a 3:1 belt-speed perturbation or tied belts (both belts: 1.5 m/s). Catch trial: To probe the magnitude of learning during adaptation,

A

Experiment 1



B

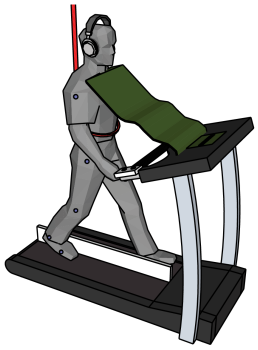


Figure 2.1 Paradigm and experimental setup diagram for speed matching task. **A**: Paradigm for Experiment 1. White blocks indicate tied belt walking (.5 m/s for both legs), grey blocks indicate split-belt walking (either both 1.5 m/s for Control Group or .5 m/s for left leg and 1.5 m/s for right leg for Split Group), and orange blocks indicate speed matching tasks (left leg .5 m/s and right leg adjusted by subject). Initially, subjects performed 3 baseline walking and speed matching task blocks, each consisting of 1 minute tied belt walking and a 30 second speed task (see Methods for task details). Next, during the adaptation block subjects either experienced a split-belt condition (Split Group) or a fast-tied condition (Control Group) for 15 minutes. Two-thirds of the way through this adaptation block a "catch trial" was introduced where *both* belts were returned to baseline speeds (.5 m/s) for 10 seconds, to assess amount of motor learning. After adaptation, both groups performed 6 speed matching tasks separated by 5 tied-belt "post-adaptation" blocks of increasing length (note: figure is not to scale). **B**: Experiment 1 speed matching task setup where subjects actively walked on the treadmill and pressed the keypad to change the speed of the right belt to match the constant left belt speed. Subject wore headphones that played white noise to cancel auditory treadmill cues and a flexible cloth drape in front of them to eliminate visual cues of feet. Infrared markers on the side of the body were used for motion capture. Physical divider separated two belts to avoid tripping. Subject also wore a safety harness in case of falling but did not support body weight.

subjects were given a brief (10 second) exposure to tied belt (.5 m/s) walking before resuming split-belt walking. Post-adaptation: all subjects walked with tied-belts (.5 m/s) to analyze motor aftereffects (i.e. how subjects unlearn the new walking pattern).

2.2.3.2 Experiment 1A - Walking Speed Perception

To investigate changes in leg speed perception due to split-belt walking, we designed a speed-matching task using the psychophysical method of adjustment. The experimental setup is shown in Figure 2.1B. Subjects were positioned on the treadmill and instructed to place their left hand on a hand rail in front of the treadmill and their right hand on a small keypad. Vision of the legs was obstructed via an opaque drape, and auditory cues of speed from the treadmill motors were cancelled via headphones playing white noise. Initially, the left leg was driven to walk at a constant speed of 0.5 m/s, while the right leg was not moving. Subjects were instructed to press up or down arrows on the keypad in front of them to adjust the speed of the right leg until they perceived it to match the speed of the left leg (reference leg). Reference leg speed was always 0.5 m/s to avoid introducing a declarative memory component to the task of remembering the reference leg speed. Subjects were given 30 seconds to complete the task, and were given feedback on the amount of time remaining via a television monitor in front of the treadmill. When the right leg was within the range 0.0 - 0.45 m/s, keypresses resulted in speed increments of either .05, .055, or .065 m/s (these increments were varied with each iteration of the task so subjects were unable to simply count the number of keypresses needed to reach the target speed). Once the speed passed 0.45 m/s, key presses resulted in a smaller change in speed, .005 m/s, to allow for fine control of speed as the right leg approached the target speed.

For Experiment 1A, subjects were randomly assigned into one of two groups: Split (n=10) and Control (n=10). The experimental paradigm is shown in Figure 2.1A. Subjects performed three periods of baseline (tied-belt walking) each followed by the speed-matching task. Next, they walked for 15 minutes in either split-belt or tied-belt conditions, with a 10 second catch trial occurring after the first 10 minutes to measure the magnitude of motor learning up to that point. Lastly, all subjects walked for 12.5 minutes with tied belts in the post-adaptation period. Walking was briefly interrupted at six time-points throughout post-adaptation so subjects could perform the speed-matching task to assess decay of sensory aftereffects over time.

2.2.3.3 Experiment 1B: Generalization of Walking Speed Perception

To determine whether perceptual speed changes after split-belt adaptation were general changes in speed perception or specific to the split-belt walking task, we modified the walking speed perception paradigm to investigate whether forward-direction split-belt walking induced perceptual speed changes in the backward walking direction (Reverse group; n=10). The paradigm was similar to that of the original walking speed perception experiment, but in addition to all of the forward walking and forward speed matching tasks, subjects also performed backwards walking and backwards speed matching tasks. Specifically, after each pair of forward baseline and forwards tasks, we added a pair of tied backwards walking (.5 m/s) and backwards speed matching tasks. The backwards walking task had the same target goal of 0.5 m/s as the original speed matching task, but occurred in the backwards direction. To measure the generalization to backwards walking in the motor domain, we also added a backwards catch trial directly

before the forward catch trial and a backwards speed matching task directly after adaptation to measure generalization in the perceptual domain.

2.2.3.4 Experiment 2 - Foot Position Perception

To investigate changes in foot position perception, we designed a position task using the psychophysical method of constant stimuli, where subjects were repeatedly asked to judge the location of their right foot relative to their left foot at various locations. Subjects were oriented on the treadmill with one leg on each belt, and were instructed to keep their left foot fixed under their trunk (as shown in Figure 2.2B). The subject's right leg was initially moved to one of three "pre-target" locations in front of the left foot, then moved to one of nine target locations uniformly distributed in front or behind the left foot (see Figure 2.2C). Once the target location was reached, subjects were instructed to verbally express whether they felt their right foot was "in front" of or "behind" their left foot. The task was repeated in a pseudorandom fashion such that each of the nine targets was visited 12 times resulting in 108 total trials. As in Experiment 1, vision of the legs was obstructed for the duration of the task, and to prevent subjects from using auditory cues to detect how far the right belt was moved to reach the target they wore headphones, which played white noise for the duration of the experiment. Right belt velocity was variable to reach each target (e.g. faster movements for farther targets) to ensure movement duration was fixed at 1.5 seconds.

The foot position perception task was performed immediately before and after 15 minutes of split-belt treadmill adaptation or tied-belt walking (Figure 2.2A). Subjects were randomly assigned to one of four groups, which performed slightly different variations of the task in order to investigate leg-specific and movement direction-specific

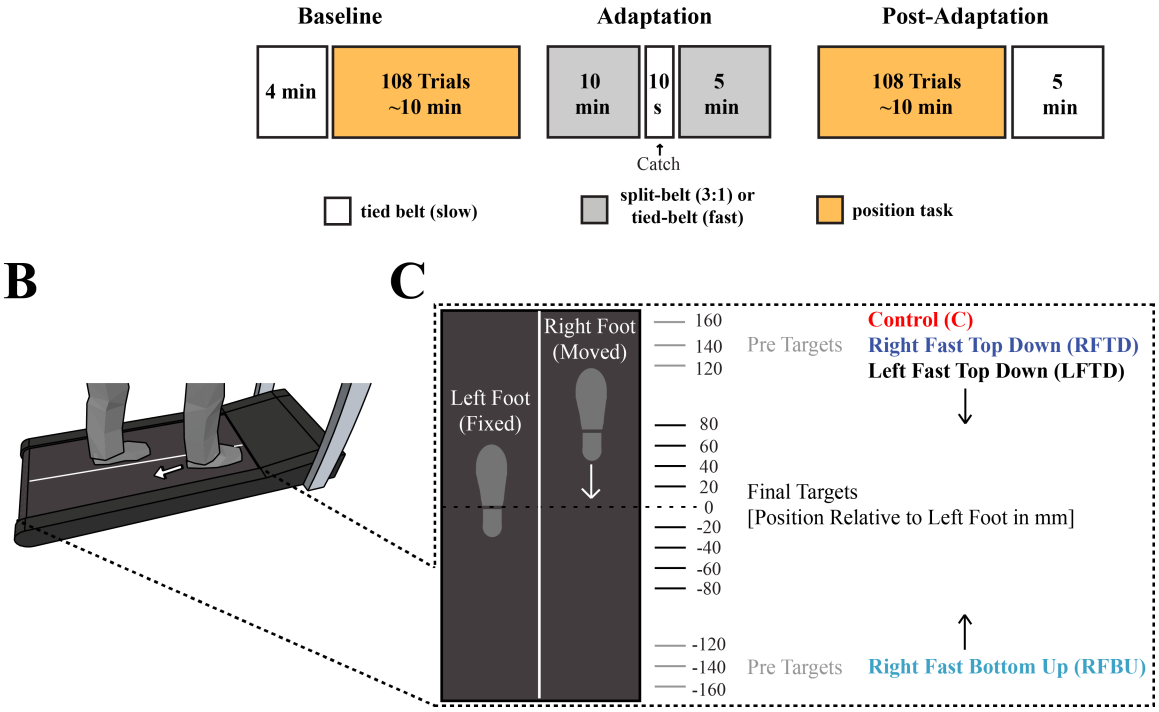


Figure 2.2 Paradigm and experimental setup diagram for position perception task. **A**: Experiment 2 paradigm. White and grey blocks represent baseline and split-belt walking with the same speeds described in Experiment 1. Orange blocks represent where the position task took place (roughly 10 min in length). Baseline walking was reduced to 4 minutes. The length of adaptation was the same as in Experiment 1. During adaptation, the Right Fast Top Down (RFTD, dark blue) and Right Fast Bottom Up (RFBU, light blue) experienced a 3:1 split perturbation with their right leg as the "fast leg". The Last Fast Top Down (LFTD, black) group experienced a 3:1 perturbation with their left leg as the fast leg. Finally, the Control group (red) walked with fast tied belts as in Experiment 1. Post-adaptation was the same as in Experiment 1. **B**: Experiment 2 position task setup was the same as in Experiment 1 except the divider was not used to eliminate extra proprioceptive cues. The subject's left foot remained at rest and the right leg was moved at every trial by the treadmill to a pre-target and then to a final target around the left foot. Subjects then proceeded to give a verbal response of whether they felt their right foot was either "in front" or "behind" their left foot.

changes. Figure 2.2C illustrates the experimental groups and their pre-target locations. The Right-Fast Top-Down (RFTD) group began the foot position perception task with the right foot moved to an initial position in front of the left foot, and split-belt adaptation was performed with the right leg as the "fast" leg. The Left-Fast Top-Down (LFTD) group performed the same task, but instead adapted with the left leg as the "fast" leg to test whether position perception changes occur more in the fast leg or slow leg. The Control group (C) performed the same task, but walked with tied belts at a speed of 1.5 m/s instead of split-belt walking (i.e. did not learn a new walking pattern). Lastly, to test whether any changes as a result of split-belt adaptation are direction dependent, the Right-Fast Button-Up (RFBU) group performed split-belt walking with the right leg as the "fast" leg (as the RFTD group did), but performed the foot position perception task with the right foot initially moved to a position behind the left foot before proceeding to the final target.

2.2.3.4.1 Foot Position Control System

Since the control unit for our split-belt treadmill is driven by speed commands, the speed task was relatively easy to implement, such that for every key press the speed in the software controller was incremented/decremented and this velocity in mm/s was sent to the treadmill controller. However, for controlling the position of one foot relative to the other we had to develop a more intricate control system to ensure we were placing the feet precisely, given that the treadmill control unit is driven by speed commands. In general, our methodology consisted of retrieving the current and desired anterior-posterior position of the ankle and then pre-calculating a trajectory and returning position and velocity pairs given a constant time of movement. This allowed us to know what the

current position and velocity should be at any time during the movement and then we used a simple type of proportional controller to compensate for any errors in position and velocity.

For the position control system we decided to move the leg such that it followed a minimum jerk trajectory. Jerk is defined as the third time derivative of position. For your nervous system to move your *smoothly* foot from one position to another, it should minimize the sum of the squared jerk along its trajectory. This is the reason we chose to use a minimum jerk trajectory for movement as it simulates how limbs are typically moved. Mathematically, the general solution for minimizing the sum of the squared jerk along a trajectory is shown in Eq.1 for position:

$$x(t) = \ a_0 + a_1 t + \ a_2 t^2 \ + \ a_3 t^3 + \ a_4 t^4 \ + \ a_5 t^5 \ \ (Eq. 1)$$

with the first time derivative (velocity) shown in Eq. 2:

$$\dot{x}(t) = \ a_1 + 2a_2 t + \ 3a_3 t^2 \ + \ 4a_4 t^3 + \ 5a_5 t^4 \ \ (Eq. 2)$$

From these known general solutions we calculated the position and velocity equations with the constraint of a constant 1.5 second movement duration. We picked this movement duration after testing various times and picking what felt like normal movement velocities by people in our laboratory as well as keeping in mind that longer times would cause the overall experimental paradigm time to change significantly since a total of 216 trials were to be executed. Also, instead of calculating the minimum jerk acceleration we found that we had to use the maximum acceleration that our treadmill is capable of in order for the controller to give precise results. Given this, the equations we derived for movement position and velocity are shown in Eq. 3 and Eq. 4:

$$x(t) = \ x_0 + (x_f - x_0) * [\ 10(\frac{t}{t_f})^3 - 15(\frac{t}{t_f})^4 + \ 6(\frac{t}{t_f})^5] \ \ (Eq. 3)$$

$$\dot{x}(t) = \ (x_f - x_0) * [\ \frac{30t^2}{{t_f}^3} - \frac{60t^3}{{t_f}^4} + \frac{30t^4}{{t_f}^5}] \ \ (Eq. 4)$$

In these equations, x_0 represents the start position (in mm), x_f represents the final position (target position, relative to fixed foot in mm), t is current time during the movement and t_f is the total duration of the movement (fixed at 1.5 seconds). The positions of the ankle markers were retrieved from our motion capture system, which has sub millimeter precision. As mentioned before, the position and velocity at every millisecond of the 1500 millisecond movement were calculated and stored in two vectors for controlling the treadmill and also for reference in the feedback compensation during the movement. The feedback compensation was employed with a simple type of proportional controller. The treadmill was controlled with a timer that was triggered every 10 milliseconds after the beginning of the movement. At each of these time points the actual position and the desired position of the ankle were retrieved and this error was used to compensate with smaller or larger velocity commands as shown in Eq. 5:

$$\dot{x}(t+1) = \ \dot{x}(t) + \ p * (x_d - x_a) \ \ (Eq. 5)$$

, where $\dot{x}(t+1)$ is the newly calculated velocity for the next time point, t is the current time during the movement, $\dot{x}(t)$ is the ideal velocity for the current time point, p is a gain coefficient, x_d is the desired position and x_a is the currently measured actual position. There were two gain coefficients used for this feedback compensation: *.05* throughout the movement and *2* for after the movement duration, each appropriately signed depending on the sign of the position error. In other words, there were some cases

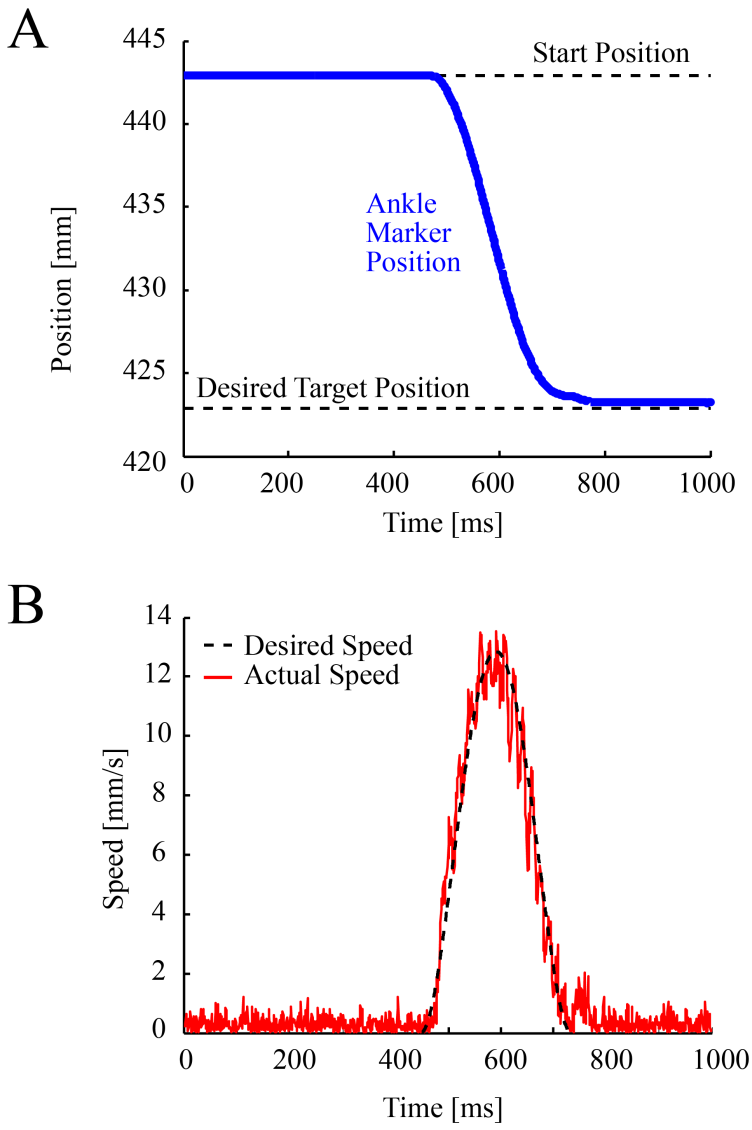


Figure 2.3 Position and speed trajectory profiles for an example 20 mm movement using the foot position control system. **A**: Actual ankle marker position (blue) and start and desired end position (black dashed lines) plotted for a 750 millisecond movement. **B**: Minimum jerk speed profile. Actual speed (red) and desired trajectory (black dashed line) are plotted

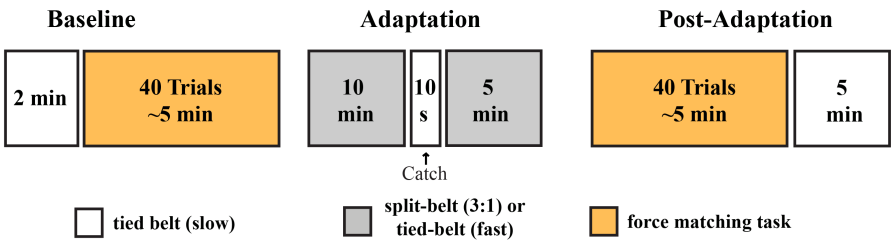
in which the subject's foot did not exactly reach the target position and for this case the gain was increased. We found that using these two values created a smooth movement throughout and also precise foot placement at the end of each trial. We tested the controller for various desired target positions and recorded ankle marker positions to verify the velocity profiles of the movements and more importantly, the position precision. We were able to verify both of these and achieve submillimeter precision. Figures 2.3A and 2.3B show example movement position and speed profiles during a typical 20 mm movement.

2.2.3.5 Experiment 3 – Stepping Force Perception

To determine whether stepping force perception changes during split-belt adaptation, we developed a stepping force perception task employing a form of the method of adjustment (see Figure 2.4B for experimental setup). Subjects were asked to adjust the amount of force when stepping on the belt with one foot and then recreate the force with the other foot. This force matching task was performed immediately before and after 15 minutes of split-belt treadmill adaptation (Split group; n=10) or tied-belt walking (Control group; n=10) (Figure 2.4A). During all walking, visual feedback of the legs was obstructed as in the previous experiments. Before any baseline walking, subjects were first instructed to stand on the treadmill so body weight could be recorded via force plates in the treadmill and to complete a training period to become familiar with the task. To perform the task, subjects were presented with one of four visual targets (a white box displayed on a screen in front of the treadmill) with varying height, representing 40%, 50%, 60%, and 70% (all ± 5%) of their body weight. For instance, when the 50% body

A

Experiment 3



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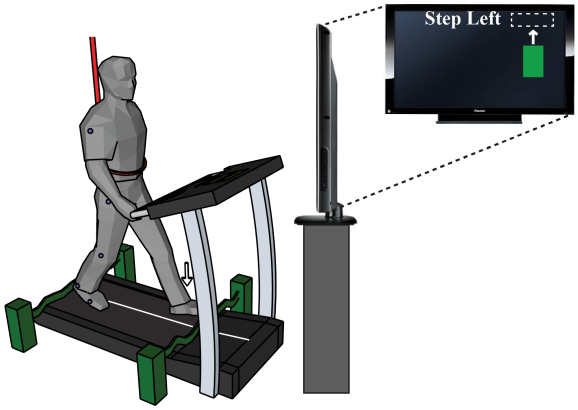


Figure 2.4 Paradigm and experimental setup diagram for stepping force perception task. **A**: Paradigm for Experiment 3. All walking portions (white and grey boxes) were the same as Experiment 2 except baseline walking was reduced to 2 minutes. Orange blocks indicate where the force task (roughly 5 minutes in length) took place. Experiment 3 only had two groups: Split Group that experienced a 3:1 perturbation with right leg as "fast leg" and a Control Group that walked with fast tied belts during adaptation, as was done in Experiment 1. **B**: Experiment 3 stepping force perception task setup. Subject stood on the treadmill in front of a television monitor where they were prompted to "step left" first and then "step right" at every trial. For the reference stepping force of each trial (done with left leg) subjects saw a target (white dashed rectangle) and a green bar increased in height depending on their stepping force. They were instructed to fluidly execute a step such that their maximum force hit the middle of the target rectangle. For the "test" stepping force (done with right leg) they were instructed to recreate the same force they exerted during the reference step but with no visual force feedback. Flexible elastic bands (shown in green) served as cues to indicate where subjects should step.

weight target was displayed, the box represented 45-55% of the subject's body weight. The following describes a typical trial made up of a "reference" step and a "test" step. In the first half of each trial, subjects were asked to perform a "reference" step in order to assess how accurately they could produce a given force with visual feedback. For these trials, the target appeared, and subjects were asked to take a step forward with their left leg, exerting force on the left treadmill belt. As force was applied to the belt, a green bar on the visual display increased in height to demonstrate the amount of force applied. Subjects were instructed to exert a force such that the height of the green bar was as close to the center of the white box as possible. In the second half of the trial, subjects performed a "test" step in order to assess how well they could remember and replicate the force exerted by the left foot during the reference trial. Unlike the reference trial, subjects did not receive visual feedback of the force applied, but were shown the same target. The entire trial (reference + test step) was repeated a total of 40 times, with each reference and test force pair executed 10 times. Elastic bands placed in front and behind the subject to give a tactile reference of distance stepped in order to fix stepping distance at approximately 16 inches.

2.2.4 Data Analysis

2.2.4.1 Motor

In all three experiments, our primary measure of adaptation in the motor domain was step symmetry – a parameter previously shown to adapt robustly during split-belt treadmill walking (Reisman et al., 2005), calculated as the difference in fast and slow step lengths, normalized to their sum to allow for comparisons across subjects who might take different-sized steps and have different leg lengths (*Eq. 6*) (Malone and Bastian,

2010). Step length was defined as the anterior-posterior distance between the ankle marker of each leg at heel strike of the leading leg (i.e. fast step length (SL_f) refers to the step length measured at fast-leg heel strike, and vice versa for slow step length (SL_s)). A step symmetry value of 0 indicates symmetric walking, and a positive value means that the fast step is larger than the slow step.

$$Step\ Symmetry = \frac{SL_f - SL_s}{SL_f + SL_s}\ (Eq. 6)$$

2.2.4.2 Walking Speed Perception

The walking speed perception task was designed to measure the ability of subjects to match the speed of their right leg to that of the left (set at a constant speed of 0.5 m/s). To assess performance, we recorded changes in right leg speed as the task was performed and quantified each subject's response to the task as the final speed of the right leg at the end of each 30 second trial.

2.2.4.3 Foot Position Perception

Foot position was measured by fitting a standard logistic function (using psignifit, see http://bootstrap-software.org/psignifit/) to each subject's responses in the position task before and after split-belt adaptation. For each foot position target, we calculated the percentage of subject responses indicating the right foot was perceived to be in front of the left. This information was used to determine the point of subjective equality (PSE: the point at which each subject's response accuracy was 50%), indicating the subject's ability to detect changes in a stimulus (in this case, changes in foot position).

2.2.4.4 Stepping Force Perception

Differences in applied stepping force between the reference force and the test force were calculated as $\Delta Force_{Test-Ref}$ for both pre and post-adaptation, where the reference leg was the right leg and the test leg was the left leg. To determine changes in force perception before and after split-belt adaptation, we calculated our main outcome parameter, $\Delta Force_{Post-Pre}$.

2.2.5 Statistical Analysis

2.2.5.1 Motor Assessments

Step symmetry was calculated at specific time-points throughout each experiment: Baseline (last 10 strides of baseline walking), Early adaptation (first 5 strides of adaptation), Catch trial (first 3 strides of catch trial), Late adaptation (last 10 strides), Early post-adaptation (first 5 strides of post-adaptation), and Late post-adaptation (last 10 strides). One-way ANOVAs or t-tests were used to compare baseline-walking averages. One-way repeated-measures ANOVAs were used to compare these six time-points with factor TIME to assess within-group changes in step symmetry during split-belt walking. We then used two-way repeated-measures ANOVAs to compare data between groups with factors GROUP and TIME. Post-hoc analysis was performed using Fisher's least significant difference (LSD) test. The Greenhouse-Geisser correction was used as needed to correct for violations of Mauchly's test of sphericity.

2.2.5.2 Sensory Assessments

Performance on sensory tasks was compared between groups using two-way repeated-measures ANOVAs with factors GROUP and TIME (Experiments 1 and 2) or GROUP and TARGET (Experiment 3). For Experiment 1, six time-points were used: the

post-adaptation time-points when the speed-matching task was performed. Baseline task averages were compared using t-tests. To compare the decay of motor and sensory aftereffects in In Experiment 1, we additionally used a two-way repeated measures ANOVA with factors MODALITY (i.e. step symmetry during either *motor* or *sensory* tasks) and TIME across the six post-adaptation time-points. In Experiment 2, pre and post-adaptation values of PSE were compared. Lastly, in Experiment 3, we compared changes in force perception at the 40%, 50%, 60%, and 70% body-weight force targets. In all cases, post-hoc analysis was performed using Fisher's LSD test. The Greenhouse-Geisser correction was used as needed to correct for violations of Mauchly's test of sphericity.

2.3 Results

2.3.1 Experiment 1

2.3.1.1 Motor learning is necessary for change in leg speed perception

We first confirmed whether subjects from the Split group learned and retained a new walking pattern and that the Control group did not. Subjects in both Split and Control groups were able to complete the walking task without difficulty. Typical single subject data is shown in Figure 2.5A. As expected, split-belt walking resulted in robust adaptation of step symmetry, while tied-belt walking resulted in no change. Group data, truncated to the lowest number of strides across groups for each walking period (baseline, adaptation, post-adaptation) are shown in Figure 2.5B for all groups (note: Reverse Group results (green) are discussed in the following section). Baseline walking step symmetry, measured by the mean step symmetry of the last 10 strides of baseline walking, was not significantly different between Split and Control groups ($p = 0.896$).

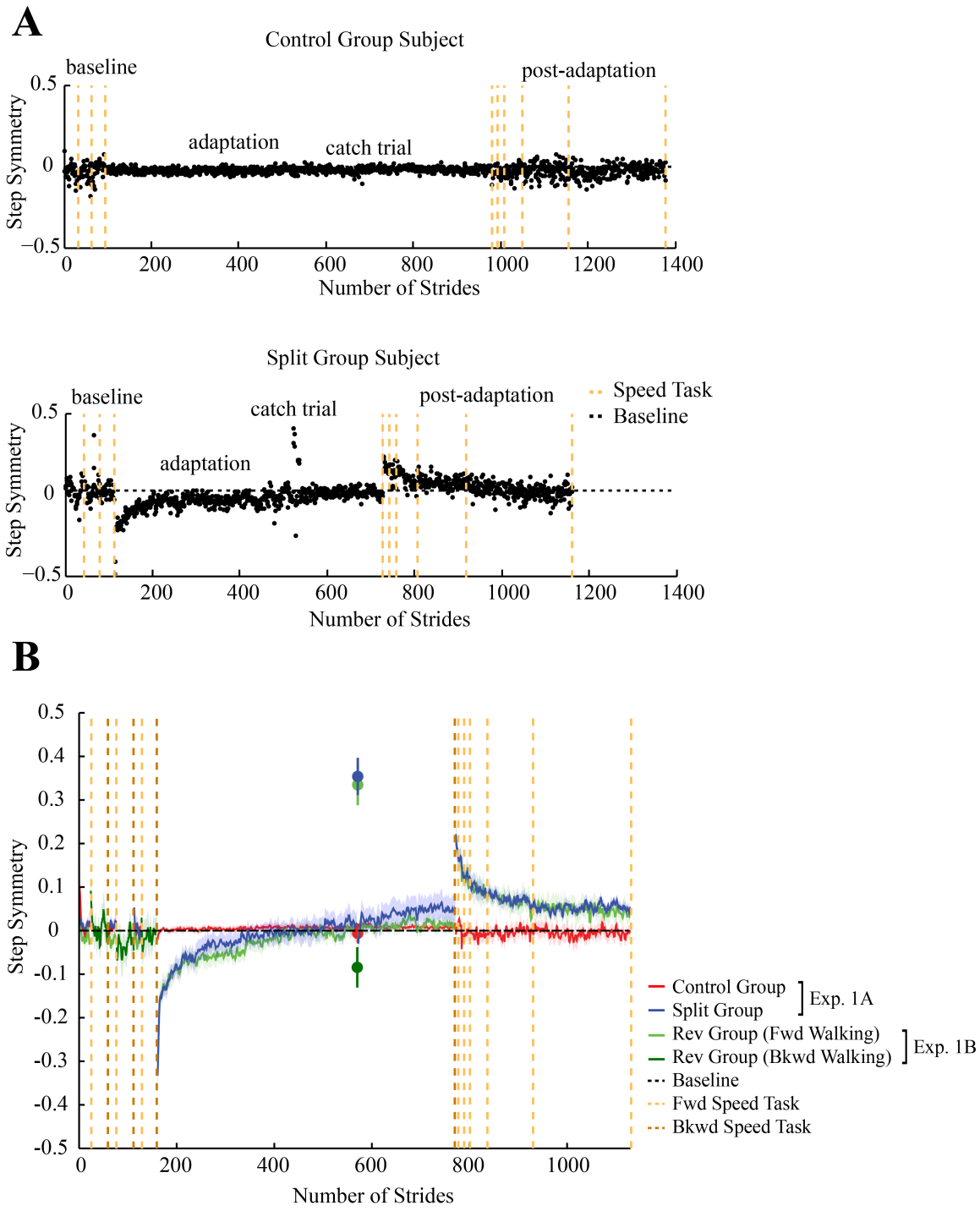


Figure 2.5 Experiment 1 motor results for all groups. **A**: Single subject data for the step symmetry parameter is shown for both a typical Control (top) and a Split Group subject (bottom) for a full experiment. Orange dashed lines represent where 30 second speed matching tasks took place. Black dashed zero line represents baseline symmetry. **B**: Group step symmetry results for the Control (red), Split (blue), Reverse Group forward walking (light green) and Reverse Group backwards walking (dark green). Curves are

smoothed with a running average of 3 strides. Shaded regions represent standard error of the mean (SEM). Closed circles represent the tied belt catch trial. Light orange dashed lines indicate where the forward walking speed matching tasks took place (all groups) and dark orange dashed lines indicates where the backwards walking speed matching tasks took place (only Reverse Group).

Analyzing changes in step symmetry across walking periods (baseline, early adaptation, catch trial, late adaptation, early post-adaptation, late post-adaptation), our one-way ANOVA demonstrated that the Split group significantly altered their step symmetry ($F(5,45) = 86.165$, $p < 0.001$), but the Control group did not ($F(5,45) = .583$, $p = 0.713$). Post-hoc comparisons in the Split group showed significant changes between baseline step symmetry and early adaptation ($p < 0.001$), catch trial ($p < .001$), early post-adaptation ($p < 0.001$), and late post-adaptation ($p = 0.025$). These results were as expected, as we have previously shown that step symmetry adapts in this manner as a result of split-belt treadmill walking (Reisman et al. 2005).

To parallel the motor adaptation result, we saw similar changes in leg speed perception as a result of split-belt walking. Specifically, while the Split group demonstrated altered performance in the speed-matching task after split-belt adaptation, no change was seen in the Control group. Typical single subject responses to the speed matching task are shown in Figure 2.6A. While both Split and Control subjects were able to match the speed of the right leg (shown in Figure 2.6A) to that of the left leg (held constant at 0.5 m/s) before adaptation, only Split group subjects exhibited changes in their response after the adaptation period. The overshoot response in the Split group subject indicates a change in leg speed perception after adaptation: the "fast" leg during adaptation (right leg) was perceived to be moving slower after adaptation. As such, Split group subjects overshot the target speed of 0.5 m/s during the post-adaptation speed perception task.

Figure 2.6B shows group speed perception data at each of the six time points the task was performed after adaptation (data shown as ΔSpeed, the size of the "overshoot"

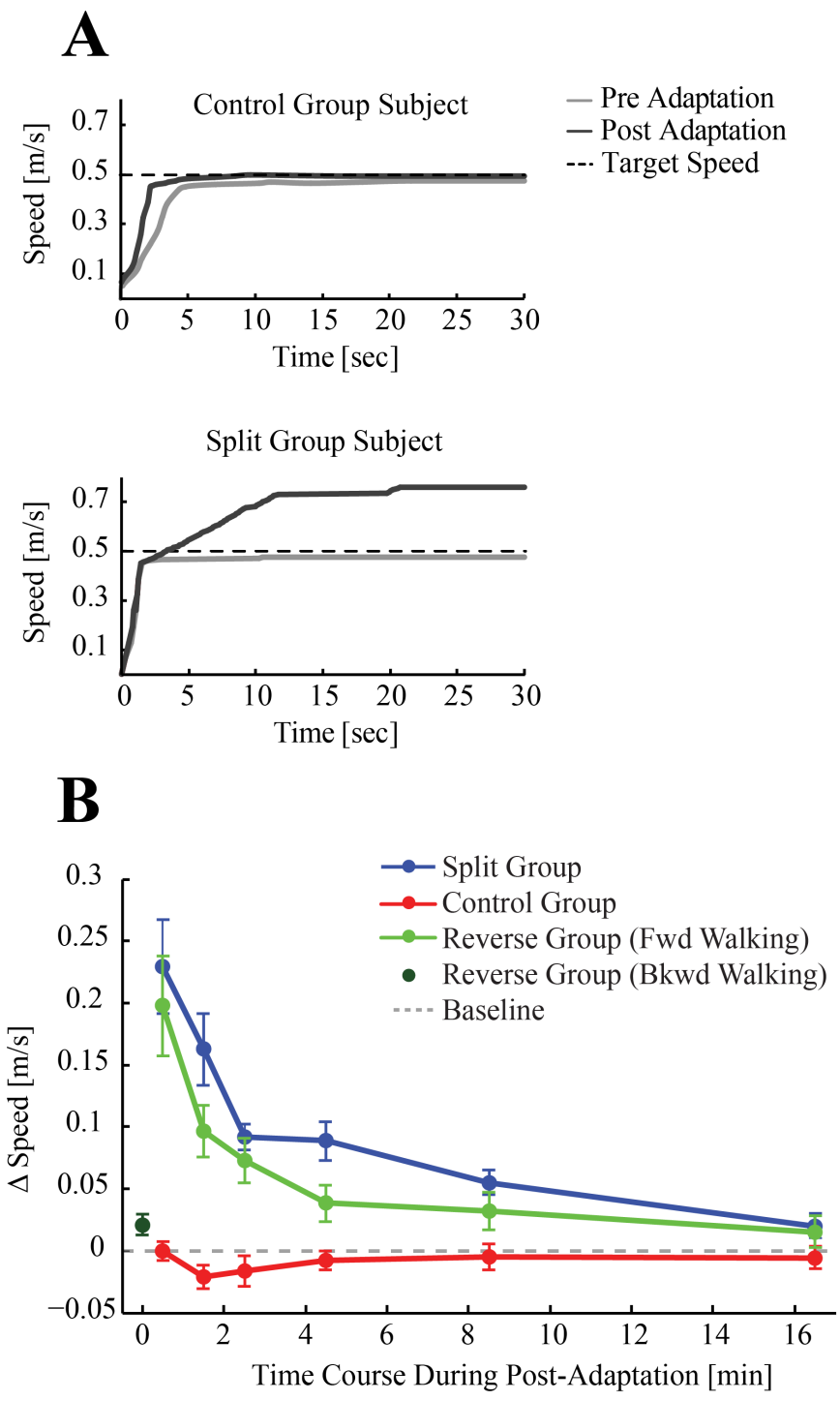


Figure 2.6 Speed matching task results for all groups (Experiment 1). **A**: Typical speed matching task responses for a Control Group subject (top) and Split Group (bottom) are shown. Subject speed adjustment responses (keypad presses) are plotted for the third baseline task (grey), initial post-adaptation tasks (black), as well as the target speed (.5 m/s) in the black dashed line. The speed at the end of each 30 second task block is the final response for that task and is used to calculate group averages. From this figure we

see that while both subjects are accurate in achieving the target speed during baseline, only the Split Group subject shows an increase in their response after adaptation, indicating a change in leg speed perception. **B**: Average group speed matching task aftereffects for Experiment 1A: Control (red) and Split (blue) and Experiment 1B: Reverse Group forward walking task (lime green) and Reverse Group backward walking task (dark green) are shown. Baseline averages (mean of 3 baselines task responses) are subtracted from the post-adaptation values. Error bars represent SEM.

in the task response). Before computing group averages shown in Figure 2.6B, each subject's baseline performance was subtracted from subsequent data for the purpose of normalization. No significant differences were found between Split and Control group baseline task performance ($p = 0.308$). Comparing post-adaptation task performance, our ANOVA showed a main effect of GROUP ($F(1,9)=47.916$, $p < 0.001$), TIME ($F(5,45)=11.156$, $p < 0.001$) and an interaction of GROUPxTIME ($F(5,45)=13.468$, $p < 0.001$). These results indicate that during post-adaptation, the Split group demonstrated changes in leg speed perception compared with the Control group that eventually decayed.

One goal of the present study was to investigate how changes in sensory perception as a result of walking adaptation might relate to changes in the motor domain. Our data suggest that both motor and sensory changes decayed on a similar time-scale (Figures 2.5B, 2.6B). Like the motor aftereffects, it appears that changes in leg speed perception took approximately 15-16 minutes to return to baseline values. However, comparing motor and sensory changes in this manner presents a problem: step symmetry is a unitless parameter, yet Δ speed is measured in m/s. As a resolution, we carried out a subsequent analysis to determine the step symmetry values for each corresponding time-point during the speed matching task. Figure 2.7 shows that the initial aftereffect in the speed matching task is approximately 52% of the initial motor aftereffect. It also shows that the time-course of motor versus sensory perceptual after-effects decay on different timescales. To analyze this further, we performed a two-way repeated measures ANOVA (six post-adaptation times points; first 5 strides of motor post-adaptation blocks and last 5 strides of each speed task) to compare the motor and perceptual decays. The ANOVA

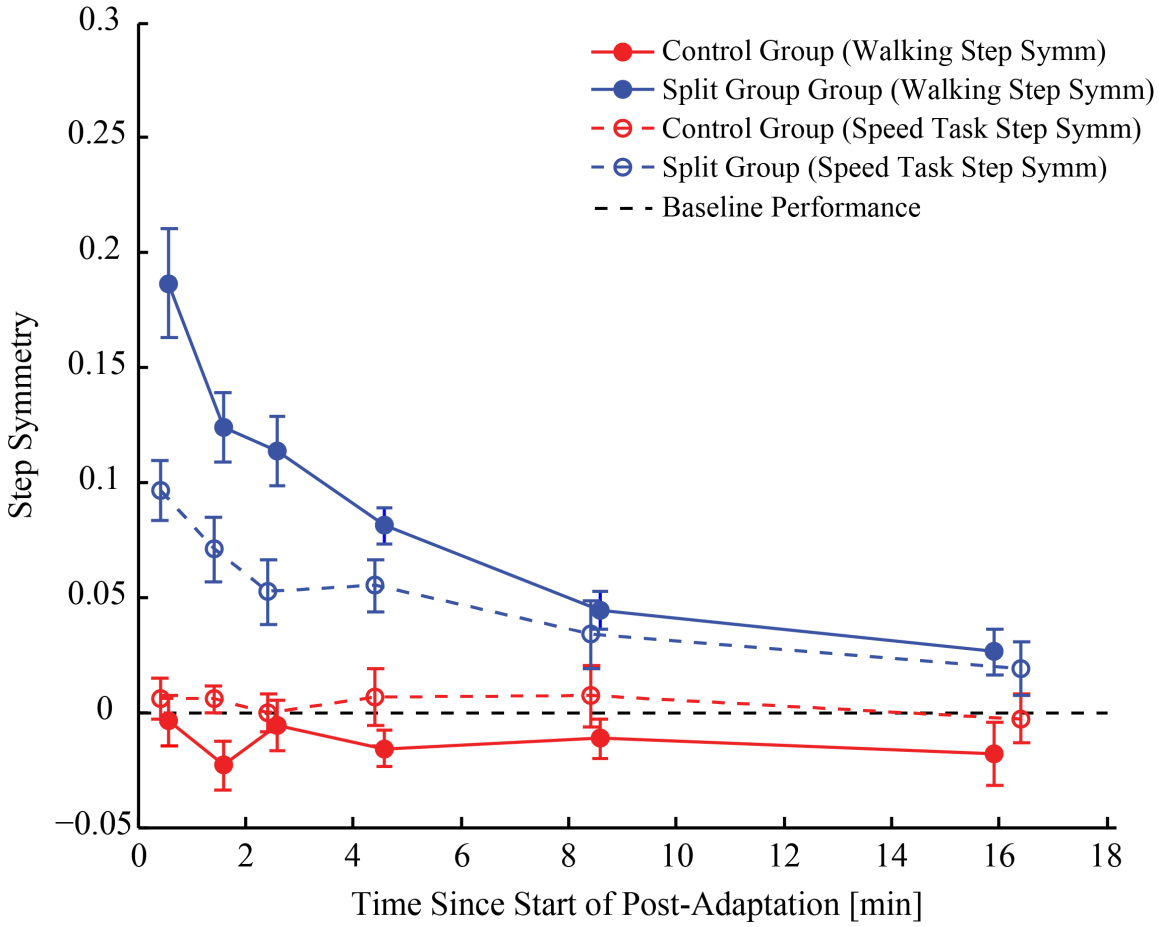


Figure 2.7 Motor and speed task motor behavior after-effect decay for Experiment 1A. Plot with group averages for the Split Group (blue) and Control Group (red) are shown for motor aftereffects (solid lines) and corresponding step symmetry at the end of each task for each group (dashed lines). Baseline averages subtracted for each. Solid lines indicate step symmetry averages (5 strides) at the beginning of all post-adaptation walking blocks and also at the end of the last block. Dashed lines and open circles indicate step symmetry averages (5 strides) at the end of each post-adaptation speed matching task. The control group showed no change. Time points 1-4 were significantly different between the motor after-effect and the speed matching effect in the Split belt group ($p < 0.05$).

showed a main effect of MODALITY ($F(1,18)= 9.556$, $p = 0.006$), TIME ($F(5,90)=28.907$, $p < 0.001$) and an interaction of MODALITYxTIME ($F(5,90)= 4.189$, $p = 0.014$). Post-hoc comparisons showed that time points 1-4 were significantly different between groups ($p < 0.05$) but time point 5 ($p = 0.103$) and time point 6 ($p = 0.124$) were not significantly different, suggesting different decay rates between motor and perceptual aftereffects. Taken together these results suggest that the motor and perceptual sensory recalibrations occur simultaneously and may be related. However, the fact that the perceptual sensory aftereffect (in terms of step symmetry) explains only about half of the motor aftereffect suggests there may be another underlying mechanism involved in learning the motor response.

2.3.1.2 Backwards Walking

Next, we asked whether forward split-belt adaptation led to a general perceptual aftereffect by testing if it transferred to the backward direction via a Reverse group. We first confirmed that baseline backwards walking performance was similar to forward walking (paired t-test, $p = 0.590$). We however found that the baseline backwards perceptual speed task was biased lower than the forward walking baseline task (paired t-test, $p = 0.001$). Our main interest however, was in observing pre to post-adaptation changes, making this difference less important. We also confirmed that both the Split and Reverse groups adapted the same amount by showing no difference in forward walking catch trial magnitude (compare light green and blue on Figure 2.5, paired t-test $p=0.811$).

We then analyzed the transfer from forward to backwards walking in the Reverse group. In the motor domain, we found small effects in the backwards catch trial step symmetry, as shown in Figure 2.5B (dark green circle, $p = 0.038$). Likewise, we found a

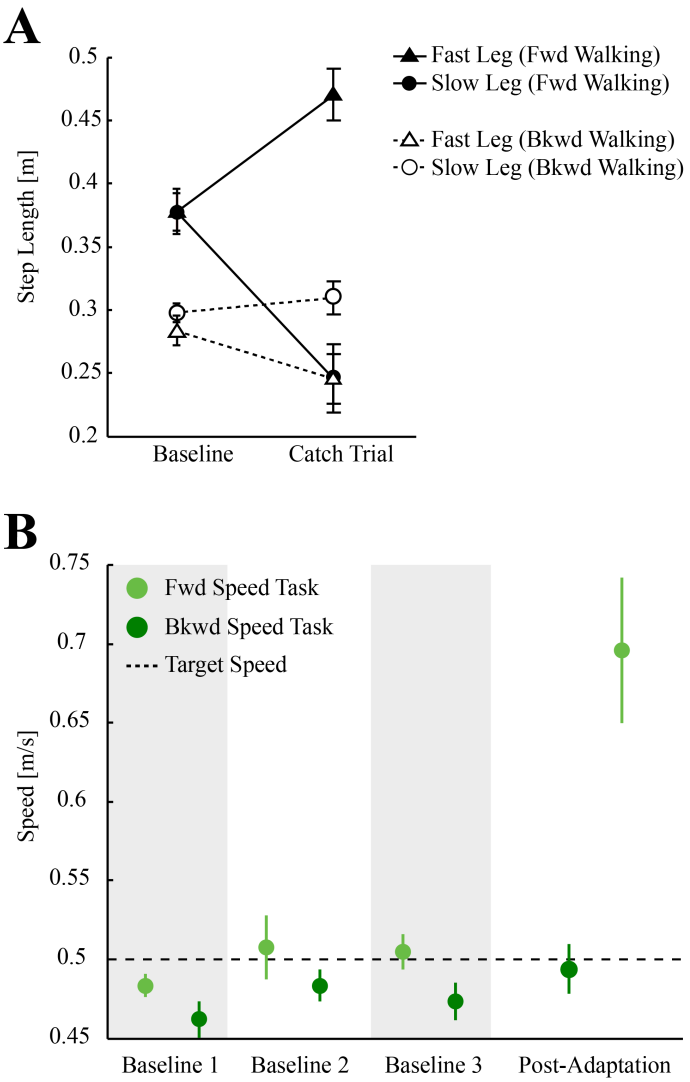


Figure 2.8 Reverse Group forward and backwards walking step length averages and perceptual speed task results (Experiment 1B). **A**: Step length averages for baseline and catch trial. Open symbols and dashed lines represent backwards walking and solid symbols and lines are forward walking. Fast leg data during adaptation (right leg) are shown as triangles and slow leg as circles. While baseline step lengths for backwards walking are shorter than forward walking, they are both symmetric. However, the forward group shows a typical aftereffect in the catch trial with a longer fast leg step and shorter slow leg step (results in a large positive step symmetry value). The backwards walking shows the opposite trend, though much smaller changes (small negative step symmetry). This suggests this is not true transfer from forward to backwards walking direction. **B**: Three baseline and initial post-adaptation averages for perceptual speed task for Reverse Group. These data show that in the backwards speed matching task, subjects tended to have a bias further away from the target speed. Importantly, the post-adaptation backwards speed task was not significantly different from the target speed ($p = .712$), suggesting this is not a true aftereffect.

very small change in the backwards speed-perception task response, as shown in Figure 2.6B (dark green symbol, $p = 0.028$). The magnitude of the backwards effects were however, closer to baseline performance than the forward walking effects. We noted that the small motor effect in backwards walking was the opposite of what we saw in the forward direction. Figure 2.8A illustrates this: during the catch trial for forward walking (closed symbols) the fast leg takes a longer step while the slow leg takes a shorter step, which is a typical aftereffect. The backwards-walking averages (open symbols) show that subjects take smaller steps and exhibit a small but opposite trend in the catch trial, with the slow leg taking the longer step. When comparing the two groups with a two-way repeated measures ANOVA we saw that there was a main effect of TIME ($F(1,18=.207$, $p < 0.001$) and also an interaction of GROUPxTIME ($F(1,18)=28.358$, $p < 0.001$). This suggests that the forward walking showed significant changes in steps lengths (from baseline to the catch trial) not present in backwards walking. This is not consistent with what would be expected for true transfer of the learned pattern to backwards walking.

We also looked carefully at the perceptual effect in backwards walking as shown in Figure 2.8B. Subjects generally improve their ability to match the leg speeds over the 3 baseline trials in both backwards and forwards walking. In the initial post-adaptation task response there is a robust perceptual aftereffect in the forward task while the backward task is not significantly different from the target speed ($p = 0.712$). This supplementary analysis seems to suggest minimal or no transfer of the perceptual after-effect from forward to backwards walking.

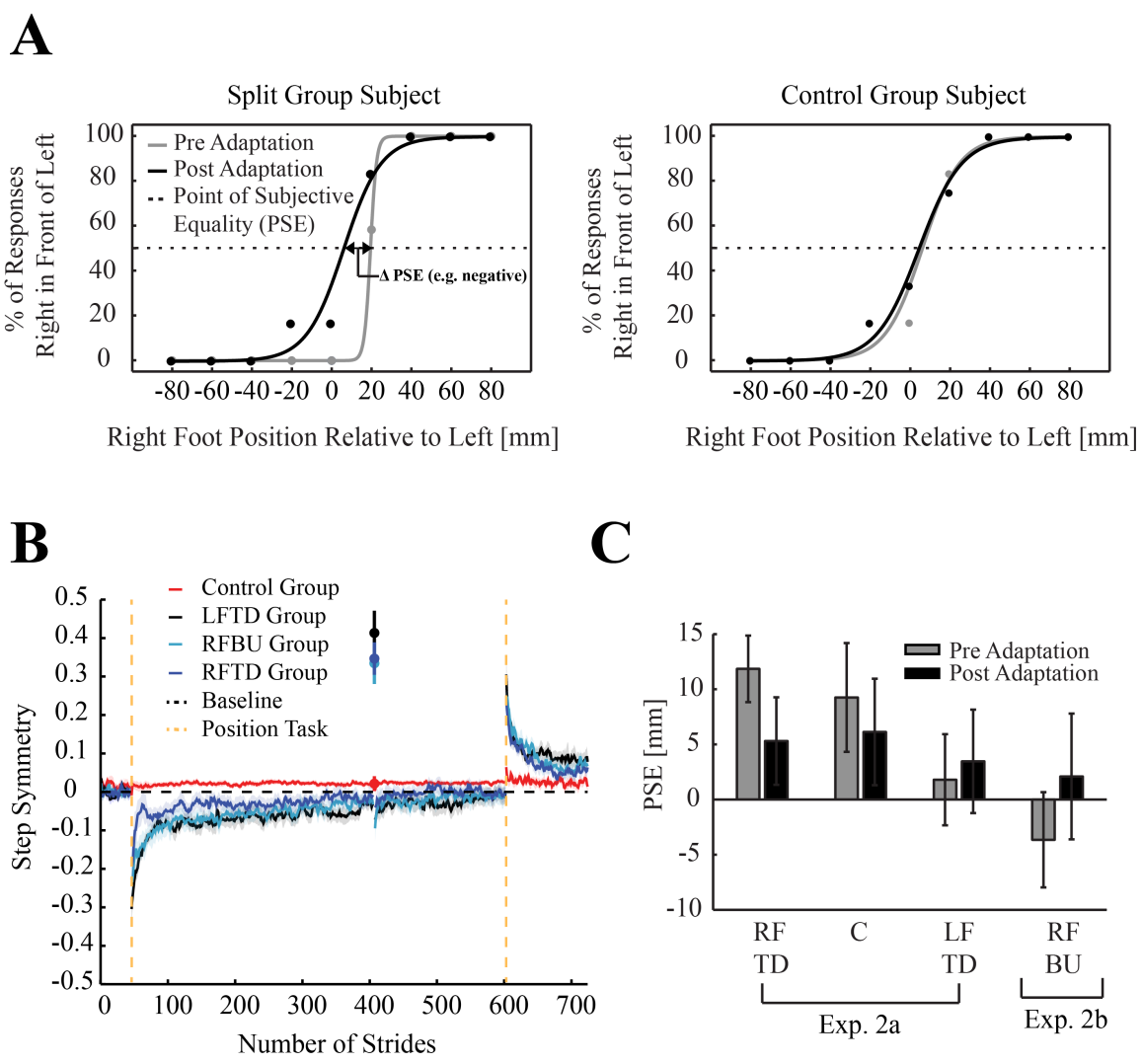


Figure 2.9 Position perception task results and corresponding motor results (Experiment 2). **A**: Representative Split Group subject (left) and Control subject (right) psychometric fits for position task for pre (grey) and post-adaptation (black). The x-axis represents the position of the right foot relative to the left foot. Each tick (9 total) is an individual final target location where subjects were asked whether their right foot was either 'in front' or 'behind' the left. The y-axis is the percentage of times the subject answered right in front of left. Logistic curves are fit to these points. The .5 mark is the point of subjective equality (PSE) and where 50% of the time they answered right in front of left. The PSE was our measure of where they perceived their foot to be located. **B**: Step symmetry values for all groups. **C**: Pre (grey) and post-adaptation (black) PSE results for Experiment 2.

2.3.2 Experiment 2 – No change in perceived foot position after adaptation

In contrast to the significant change in leg speed perception found in Experiment 1, we found no significant difference in perceived foot position after split-belt adaptation. Motor behavior for all four groups is shown in Figure 2.9B. Repeated measures ANOVA showed main effects of GROUP ($F(3,36)=5.130$, $p =.005$), TIME ($F(5,180) = 114.635$, $p < 0.001$), and a GROUPxTIME interaction ($F(15,180) = 13.292$, $p < 0.001$) for step symmetry. As expected, post-hoc tests revealed that the Control group was significantly different from the RFTD group ($p = 0.003$), LFTD group ($p = 0.001$) and the RFBU group ($p = 0.011$), but no significant differences were found between the RFTD, LFTD and RFBU groups.

Typical single subject responses and logistic fits for the foot position perception task are shown in Figure 2.9A. Logistic fits for each task for all of the subjects had significant goodness of fit (as measured by deviance values in psigniFit). Group changes in point of subject equality (PSE) pre and post-adaptation are shown in Figure 2.9C. In general, data showed that subjects who performed the task in the top-down direction (RFTD, C, and LFTD) had a positive PSE bias (i.e. they perceived the right leg to be positioned more posteriorly than it actually was), and the bottom-up group (RFBU) demonstrated a negative bias. However, our ANOVA showed no main effect of GROUP ($F(3,27)=1.015$,$p = 0.401$) or TIME ($F(1,9)=.287$, $p = 0.605$), but revealed a significant GROUPxTIME interaction ($F(3,27)=145.614$, $p= 0.013$). Post-hoc analysis did not show any significant differences between individual groups. Taken together, these results demonstrate that split-belt adaptation did not produce significant changes in foot position perception.

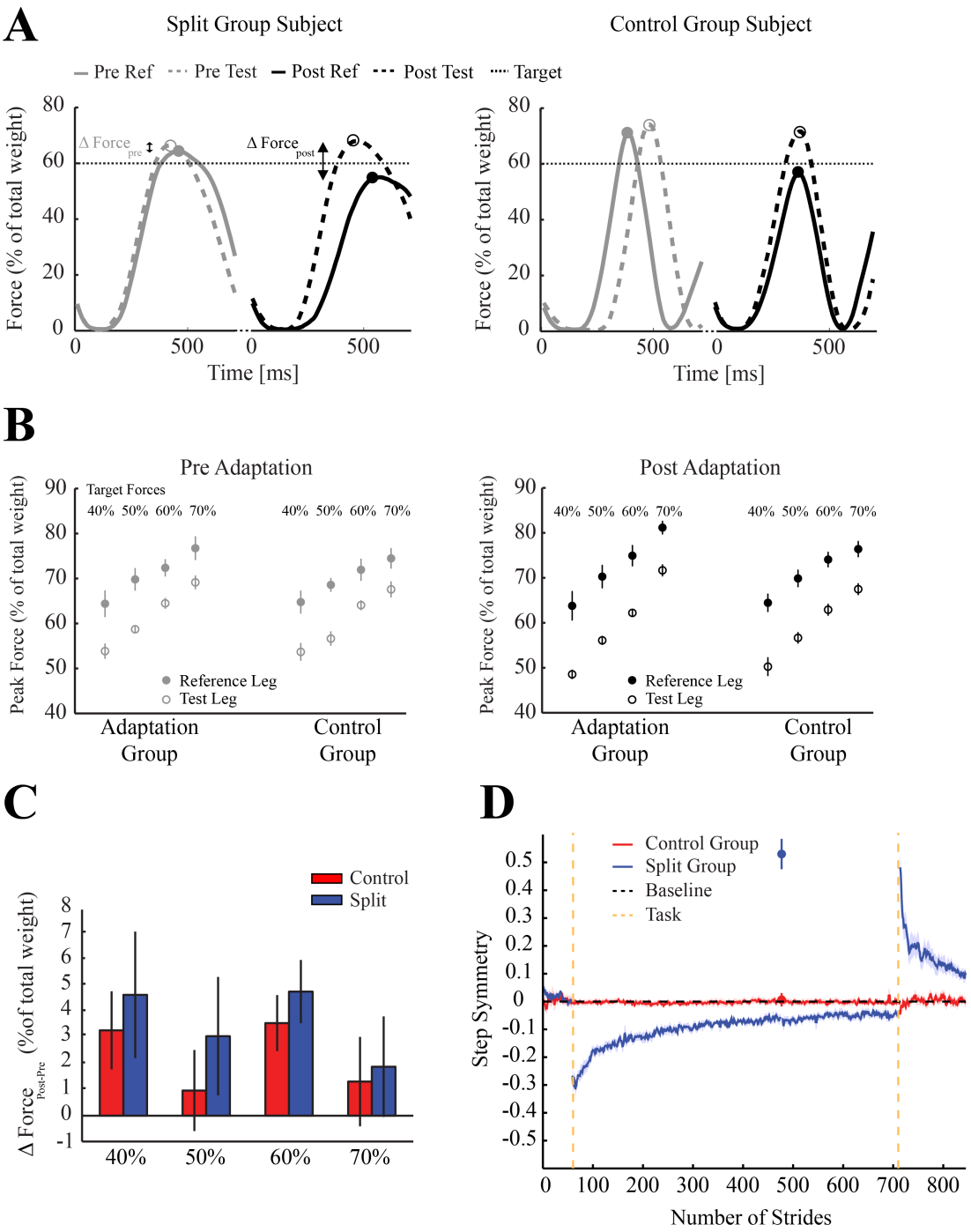


Figure 2.10 Force matching perception task results and corresponding motor results (Experiment 3). **A**: Representative single trial stepping force (as percentage of body weight) trajectory data for a Split Group subject (left) and Control Group subject (right). Circles show example peak forces that are extracted to use as final response for each trial. Solid curves represent the reference force trajectories (with visual feedback) and dashed curves represent opposite test leg force trajectories (without visual feedback). Grey curves are pre-adaptation and black curves are post-adaptation data. **B**: Group peak force

averages for all 4 stepping force targets for reference leg (filled circles) and test leg (open circles) for both pre (left) and post-adaptation (right). Reference leg forces are closer to desired targets than the test leg but both showed overshooting, especially on the lower percentage targets. **C**: $\Delta \mathrm{Force}_{\mathrm{Post-Pre}}$, the main parameter used to quantify how force perception changes as a result of adaptation, is shown for all targets. **D**: Group step symmetry averages for the Control Group (red) and Split Group (blue). As expected, the split group shows typical adaptation and retention of the walking pattern while the control does not show any changes.

2.3.3 Experiment 3 – No change in perceived foot force production after adaptation

Similar to the results of foot position perception, we found no differences in stepping force perception after split-belt adaptation. Specifically, we investigated changes in stepping force perception between the two legs pre and post-adaptation. Motor adaptation results, shown in Figure 2.10D, were consistent with findings of Experiment 1 and 2. Typical single subject stepping force curves for a 60% target trial and group peak force measurements at each target are shown in Figures 2.10A and 2.10B, respectively. For 40%, 50% and 60 % targets, subjects in both groups tended to overshoot force on the reference leg, but this overshoot was much more pronounced in the test leg. Figure 2.10C shows group data for pre/post-adaptation changes in our main force perception parameter, $\Delta Force_{Post-Pre}$. Our ANOVA did not show significant main effects of GROUP ($F(1,72) = .985$, $p = 0.324$), TARGET ($F(3,72)= 0.999$, $p = 0.399$), or GROUPxTARGET ($F(3,72)=0.056$, $p = 0.983$) interaction, indicating that split-belt adaptation did not produce significant changes in stepping force perception compared to tied-belt walking.

2.4 Discussion

Here we show that split-belt adaptation leads to kinesthetic changes in leg speed perception during walking, but not foot position in standing or stepping force. Specifically, the leg that moved faster during adaptation is perceived to move slower afterwards. This perceptual aftereffect is robust, decays with unlearning of the motor behavior, and is specific to the learned direction of walking.

We were surprised to find that sensory changes resulting from split-belt adaptation were specific to leg speed perception and did not occur for perceived static

foot position or stepping force. While split-belt treadmill walking mainly causes a perturbation in leg speed, it also perturbs the position of the feet at heel strike and toe off, as well as ground reaction forces during walking (Mawase et al., 2013). Our previous work (Malone and Bastian, 2010) shows that like step symmetry, the angle about which the legs oscillate (an indicator of foot position) is initially perturbed, adapts, and shows robust aftereffects with split-belt walking. As such, we expected that this kinematic change would occur alongside a comparable change in perceived foot position. However, this was not the case. One possible explanation for our null result is the passive nature of our foot position task. Subjects were asked to make judgments of the location of their feet after being passively moved by the treadmill, which may have been too dissimilar from the active stepping context of walking to reveal any changes in the sensory domain. Further, our previous work demonstrated that the cerebellum is vital for proprioception of active, self-driven movements, but not passive movements (Bhanpuri et al., 2013). One might thus expect that after learning a cerebellar-dependent motor task such as split-belt walking, probing position perception or stepping force with an active movement might be more likely to result in significant changes.

The present study expands on previous work demonstrating that leg speed perception is recalibrated during split-belt treadmill walking. In particular, Jensen et al. (1998) showed that split-belt adaptation results in a fairly immediate change in the perception of leg speed such that the "fast" leg during adaptation feels slower after adaptation. Here we additionally show that rather than a transient change, this sensory aftereffect gradually decays over a period of 5-15 minutes on a similar timescale (albeit likely different rate) of motor aftereffects. Further, by expressing it in terms of a known

motor parameter (m/s; see Figure 2.7), we demonstrate that the sensory aftereffect does not fully account for the motor aftereffect. In fact, the initial sensory aftereffect represents only approximately 50% of the magnitude of the motor aftereffect and converges with the motor aftereffect after approximately 6-8 minutes of washout. Other mechanisms, such as use-dependent plasticity and explicit control of walking, may explain the residual motor aftereffects not accounted for by the sensory recalibration.

Our results also show that both the motor and sensory consequences of split-belt adaptation are unique to the direction of adaptation. In other words, forward-direction adaptation has minimal to no aftereffects in the backward direction. This result builds upon previous findings that the motor aftereffects of split-belt walking are direction-specific (Choi & Bastian, 2007). It should be noted that our current work shows very small transfer in the motor and perceptual domains, but our additional analysis suggests that these effects may be due to other factors. The small motor after-effect during walking is in the opposite direction that was trained, which suggests another mechanism might at play. The perceptual effect could be explained by subjects initial baseline bias (underestimate) that improved with practice. After forward adaptation subjects showed no perceptual aftereffect in backward walking.

While we have shown that locomotor adaptation only affects perception of leg *speed*, studies of the sensory consequences of reaching adaptation have primarily focused on changes in felt hand *position*. For instance, Salomonczyk and colleagues (2011) showed that adaptation to an abrupt, 30 degree visuomotor rotation resulted in a 7.3 degree shift in perceived hand position – a 24.3% change relative to the size of the

perturbation. Our subjects, on the other hand, exhibit a change in perceived foot position of only 7 mm. It has been recently suggested that a split-belt treadmill perturbation with a 3:1 belt speed ratio, like the one used in this study, results in a spatial perturbation of 200 mm (Finley et al., 2015). As such, this 7 mm change in position perception can be quantified as a negligible 3.4% of the size of the perturbation. Leg speed perception, however, appears to be a much more salient percept for split-belt walking. Subjects in the Split group of Experiment 1 exhibited a .216 m/s change in perceived leg speed compared with baseline performance. Given the speed perturbation size of 1 m/s (the difference in the belt speeds during adaptation), this change in perception can be quantified as 21.6% - much closer to that of hand position perception found in the aforementioned reaching study. Considering that force field reaching adaptation studies frequently use perturbations that are velocity dependent (Haith et al., 2008; Ostry et al., 2010; Mattar et al., 2013), we were surprised to find that the effect of reaching adaptation on hand velocity perception has yet to be investigated. We speculate that determining this relationship would help inform us on the difference in control systems between reaching and walking adaptation.

The underlying mechanisms driving the change in leg speed perception following split-belt walking have yet to be determined. Anstis et al. (1995) showed that simply jogging on a regular treadmill can produce changes in perceived movement speed, suggesting a possible connection between sensory recalibration and use-dependent processes. Given that our split-belt subjects exhibited perceptual aftereffects but control subjects did not, we interpret the sensory recalibration we observed to be closely tied to the error-driven, cerebellar dependent motor adaptation that occurs during split-belt

walking. Along these lines, Izawa et al. (2012) and Synofzik et al. (2008) have argued that in reaching adaptation, recalibration of perceptual estimates are cerebellar-dependent. On the other hand, Henriques et al. (2014) suggested the above studies may have seen cerebellar patient deficits that are not purely due to a failure in predicting sensory consequences, as this is hard to measure. They state that these deficits might also be due to changes in felt hand position (pure proprioceptive recalibration) rather than exclusively efferent-based predictions. That explanation seems unlikely -- if a general proprioceptive recalibration occurred we might expect to see changes in the perceived speed of backward walking, which we did not. It is well known that the cerebellum is necessary for updating a forward model and driving locomotor adaptation (Morton and Bastian, 2006; Jayaram et al., 2011; Jayaram et al., 2012), and plays a critical role in sensory perception of active hand movements (Bhanpuri et al., 2013). Given this, as well as the fact that the sensory recalibration we observed was dependent on concurrent motor adaptation, we favor the possibility that the cerebellum plays an important role in the recalibration of leg speed perception we demonstrate in the present study.

We have shown that split-belt treadmill adaptation leads to changes in active leg speed perception, but not perceived foot position or stepping force. Further, we have demonstrated that the sensory changes resulting from split-belt adaptation are specific to the direction of learning. We speculate that the cerebellum plays a critical role in the effects we observed, and suggest that testing these concepts on patients with cerebellar lesions may help elucidate the mechanisms underlying the sensory consequences of locomotor adaptation.

CHAPTER 3

Cerebellar Contributions to Motor and Perceptual Recalibration

3.1 Introduction

To compensate for delayed sensory feedback, it is thought that the brain predicts the sensory consequences of movement in order to make better goal-oriented movements (Körding & Wolpert, 2004; Shadmehr et al., 2010; Vaziri et al., 2006). This association between outgoing motor commands and their consequences is commonly referred to as a forward model. The disruption of such a forward model can lead to movement deficits such as ataxia (i.e. an incoordination of movements). In arm movement, it has been suggested that a putative neural location for a forward model is the cerebellum, as temporary disruption or developmental damage to the cerebellum have been shown to induce deficits in sensory predictions of motor commands (Miall et al., 2007; Nowak et al., 2007). As a consequence of such sensory prediction deficits, numerous studies have found degraded performance in reaching adaptation (Manto et al., 1994; Maschke et al., 2004; Smith & Shadmehr, 2005). The cerebellum has additionally been shown to be important in split-belt walking adaptation for predictive but not reactive locomotor adjustments (Morton & Bastian, 2006), and the rate of locomotor adaptation can be modulated through non-invasive direct-current stimulation of the cerebellum (Jayaram et al., 2012). Overall, these studies demonstrate the importance of the cerebellum in motor adaptation.

Recent studies in reaching have shown that in addition to recalibration in the motor domain, motor adaptation can lead to changes in sensory perception, including changes in perceived hand position and motion during reaching adaptation (Cressman & Henriques, 2009; Haith et al., 2008; Mattar et al., 2013; Ostry et al., 2010; Salomonczyk et al., 2011, 2012). While the cerebellum is known to be vitally important to these forms of motor adaptation, there is no consensus in the literature regarding the influence of the cerebellum on the sensory consequences of motor adaptation. Some studies have shown that patients with cerebellar damage exhibit deficits in the sensory recalibration that would normally occur alongside motor adaptation (Izawa et al., 2012; Synofzik et al., 2008), yet others have found no impairment compared with controls (Henriques et al., 2014).

In the present study, we are interested in investigating the role of the cerebellum in a form of perceptual sensory recalibration which occurs alongside split-belt treadmill adaptation. It has been previously shown that split-belt walking can induce changes in leg speed perception in healthy adults (Jensen et al., 1998). Henriques et al. (2014) argue that it may be difficult to dissociate predictive estimates and sensory estimates of hand movement in volitional reaches due to the strong interaction between visual and proprioceptive feedback which drive recalibration in reaching adaptation paradigms. However, we believe split-belt adaptation is more reliant on the proprioceptive sense given that less explicit visual feedback of performance is used in walking compared to reaching adaptation paradigms. As such, it may be easier to investigate how predictive and sensory estimates of leg speed change during split-belt adaptation without confounding cross-sensory interaction with vision.

Examining the spatial versus temporal characteristics of walking may further help us determine the involvement of the cerebellum in motor and perceptual sensory recalibration. We have previously suggested that the cerebellum may be more involved with the control of the spatial component of walking adaptation (i.e. where the foot is placed), as opposed to the temporal component (i.e. when the foot is placed) (Jayaram et al., 2012; Malone et al., 2011; Patrick et al., 2014). However, we do not currently know the spatiotemporal contributions of split-belt adaptation in regards to changes in leg speed perception. In other words, is recalibration of leg speed perception more reliant on spatial or temporal components of adaptation? If perceptual sensory changes are directly related to cerebellar function, we would expect patients with cerebellar damage to exhibit reduced perceptual aftereffects alongside diminished spatial motor aftereffects. Alternatively, if sensory recalibration processes are independent of the cerebellum (e.g. if they are more closely related to use-dependent learning, rather than error-driven motor adaptation), we would not expect any differences in recalibration of leg speed perception between healthy controls and patients with cerebellar damage.

To investigate the contributions of the cerebellum to concurrent changes in motor and sensory recalibration, we tested the ability of patients with cerebellar ataxia to both adapt to a split-belt treadmill and perform a speed matching task to test leg speed perception during walking. We hypothesized that the cerebellum plays an important role in recalibration in both the motor and perceptual domains. Thus, we expected that patients with cerebellar damage would exhibit diminished motor aftereffects of split-belt walking (as seen in Morton & Bastian, 2006), and this would occur alongside impaired recalibration of leg speed perception.

3.2 Materials and Methods

3.2.1 Subjects

A total of sixteen, right hand and right leg dominant, volunteers (7 males and 9 females; mean age, 62 yrs old +/- 13) participated in this study. Cerebellar ataxia patients (Cerebellar group; n=8) were recruited from our laboratory database. Two of the patients were naive to the treadmill, meaning they had never experienced a split belt treadmill, and the other six had not walked on a split-belt treadmill for at least 6 months prior to the experimental session. Neurological and motor deficits were quantified with the International Cooperative Ataxia Rating Scale (ICARS; Trouillas et al., 1997). Table 3.1 is a summary of information regarding our subjects' age, gender, relevant neurological exam scores, and diagnoses. Healthy, age-matched (within 5 years) control participants (Control group; n=8) had no self-reported history of relevant neurological, and/or motor dysfunction. The protocols were approved by the Johns Hopkins Institutional Review Board and all participants provided written informed consent before testing.

3.2.2 Experimental Setup

Split-belt treadmill walking. Split-belt walking adaptation was studied using a custom-built treadmill (Woodway, Waukesha, WI) with two separate belts driven by independent motors. Speed commands for each belt were sent to the treadmill through either a custom MATLAB (The MathWorks, Natick, MA) program or a custom Python program in the Vizard (WorldViz, California USA) development environment, depending on the task performed by the subject. Vertical forces exerted on each belt were recorded at 1000 Hz. Subjects wore a safety harness which did not support their body weight during walking and were positioned in the middle of the treadmill with one leg on each belt. A wooden divider separated each belt so legs stayed on their respective belts.

Subject	Age	Gender	Diagnosis	ICARS Total	ICARS Gait/Posture
CBLR-1	61	M	ADCA	14	8
CBLR-2	69	F	Sporadic	19	12
CBLR-3	64	F	L SCA	23	11
CBLR-4	59	F	Sporadic	35	12
CBLR-5	79	M	Sporadic	32	11
CBLR-6	74	M	Sporadic	42	25
CBLR-7	32	F	R CBLR Stroke	23	9
CBLR-8	62	F	Sporadic	43	18
CBLR Avg	**62.5 +/- 14.1**	-	-	**28.875**	**13.25**
Control Avg	**61 +/- 12**	-	-	-	-

Table 3.1 Subject demographics. ICARS, International Cooperative Ataxia Rating Scale; CBLR, cerebellar subject; F, female; M, male; R, Right; L, Left; ADCA, autosomal dominant cerebellar ataxia; Sporadic, sporadic adult-onset cerebellar ataxia; SCA, spinocerebellar ataxia;

Optotrak motion analysis. Kinematic data were collected at 100 Hz using Optotrak (Northern Digital, Waterloo, ON, Canada). Bilateral infrared-emitting markers were placed over the toe (fifth metatarsal head), ankle (lateral malleolus), knee (lateral femoral epicondyle), hip (greater trochanter), pelvis (iliac crest), and shoulder (acromion process).

Speed Matching Task. We studied sensorimotor perception of walking speed before and after split-belt walking at various time points. Custom Python programs were used to control the treadmill, provide feedback of task timing, and collect subjects' responses. Details for the speed matching task are in the following section.

3.2.3 Experimental Protocols

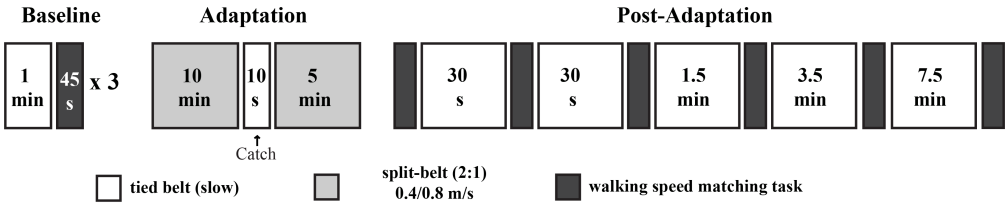
3.2.3.1 Split-Belt Walking Adaptation

The general experimental paradigm is shown in Figure 3.1A. All subjects began with 3 baseline periods (1 min. each) during which the belts were tied at 0.4 m/s. Subjects were then exposed to a 15 minute period of split-belt walking (belts split at 0.4 and 0.8 m/s for left and right belts, respectively). After the first 10 minutes of adaptation, subjects experienced a 10 second "catch" trial, where the belts were again set to 0.4 m/s. This catch trial enabled us to probe the magnitude of learning in the middle of the adaptation period. After the catch trial, subjects resumed split-belt walking for another 5 minutes. During post-adaptation, subjects walked at tied belts (0.4 m/s) for a total of 13.5 minutes, intermittently performing the speed matching task during post-adaptation.

3.2.3.2 Speed Matching Task Details

To assess changes in leg speed perception due to split-belt adaptation, we asked subjects to perform a walking speed matching task (similar to Jensen et al., 1998) after

A



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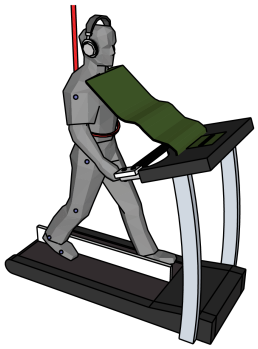

Figure 3.1 Paradigm and experimental setup diagram for speed matching task. **A**: Paradigm. White blocks indicate tied belt walking (0.4 m/s for both legs), light grey blocks indicate split-belt walking (0.4 m/s for left leg and 0.8 m/s for right leg), and dark grey blocks indicate speed matching tasks (left leg 0.4 m/s and right leg adjusted by subject). Initially, subjects performed 3 baseline walking and speed matching task blocks, each consisting of 1 minute tied belt walking and a 45 second speed task (see Methods for task details). Next, during the adaptation block subjects experienced a split-belt condition for 15 minutes. Two-thirds of the way through this adaptation block a "catch trial" was introduced where *both* belts were returned to baseline speeds (0.4 m/s) for 10 seconds, to assess amount of motor learning. After adaptation, both groups performed 6 speed matching tasks separated by 5 tied-belt "post-adaptation" blocks of increasing length (note: figure is not to scale). **B**: Speed matching task setup where subjects actively walked on the treadmill and pressed the keypad to change the speed of the right belt to match the constant left belt speed. Subject wore headphones that played white noise to cancel auditory treadmill cues and a flexible cloth drape in front of them to eliminate visual cues of feet. Infrared markers on the side of the body were used for motion capture. Physical divider separated two belts to avoid tripping. Subject also wore a safety harness in case of falling but did not support body weight.

each baseline period and intermittently throughout post-adaptation (see Figure 3.1A). The experimental setup is shown in Figure 3.1B. Subjects were positioned on the treadmill and instructed to place their left hand on a hand rail in front of the treadmill and their right hand on a small keypad. Vision of the legs was obstructed via an opaque drape, and auditory cues of speed from the treadmill motors were cancelled via headphones playing white noise. Initially, the left leg was driven to walk at a constant speed of 0.4 m/s, while the right leg was not moving. Subjects were instructed to press up or down arrows on the keypad in front of them to adjust the speed of the right leg until they perceived it to match the speed of the left leg (reference leg). Reference leg speed was always 0.4 m/s to avoid introducing a declarative memory component to the task of remembering the reference leg speed. Subjects were given 45 seconds to complete the task, and were given feedback on the amount of time remaining via a television monitor in front of the treadmill. When the right leg was within the range 0.0 - 0.35 m/s, keypresses resulted in speed increments of either .05, .055, or .065 m/s. These increments were varied with each iteration of the task so subjects were unable to simply count the number of keypresses needed to reach the target speed. Once the speed passed 0.35 m/s, key presses resulted in a smaller change in speed, .005 m/s, to allow for fine control of speed as the right leg approached the target speed.

3.2.4 Data Analysis

3.2.4.1 Spatiotemporal Motor Parameters

The primary outcome measures of motor behavior were step symmetry, phasing, and center of oscillation, which have all been shown to adapt robustly during split-belt walking in healthy adults (Choi & Bastian, 2007; Jayaram et al., 2012; Malone &

Bastian, 2010; Reisman et al., 2005). While step symmetry (Figure 3.2A) is considered a global, spatiotemporal measure of walking coordination, phasing (Figure 3.2D) and center of oscillation (Figure 3.2C) were used to determine the distinct spatial (center of oscillation) versus temporal (phasing) contributions to adaptation.

Step symmetry was calculated as the difference in fast and slow step lengths, normalized to their sum to allow for comparisons across subjects who might take different-sized steps or have different leg lengths (Malone & Bastian, 2010). Step length (Figure 3.2B) was defined as the anterior-posterior distance between the ankle (lateral malleolus) marker of each leg at heel strike of the leading leg; fast step length refers to the step length measured at the fast-leg heel strike, and vice versa.

Changes in step symmetry can be achieved by altering the spatial and/or temporal components of walking. The measure of spatial coordination, center of oscillation, was calculated as the midpoint of the limb angle between heel strike and toe off for each leg (Malone & Bastian, 2010). A center of oscillation value of zero indicates symmetric oscillation of the legs under the trunk. In our analysis, we subtracted the center of oscillation of the fast leg from that of the slow leg to give the center of oscillation difference (COD) between the legs.

Phasing, the temporal component of walking, was determined using the time series of limb angles for each leg. It is quantified as the lag time at peak cross-correlation (Signal Processing Toolbox, MATLAB) of the limb angle trajectories over one stride cycle, with reference to the slow leg (Choi & Bastian, 2007). Ranging from values of 0 to 1, symmetric phasing (i.e. exact anti-phase movement between the legs) is indicated by 0.5.

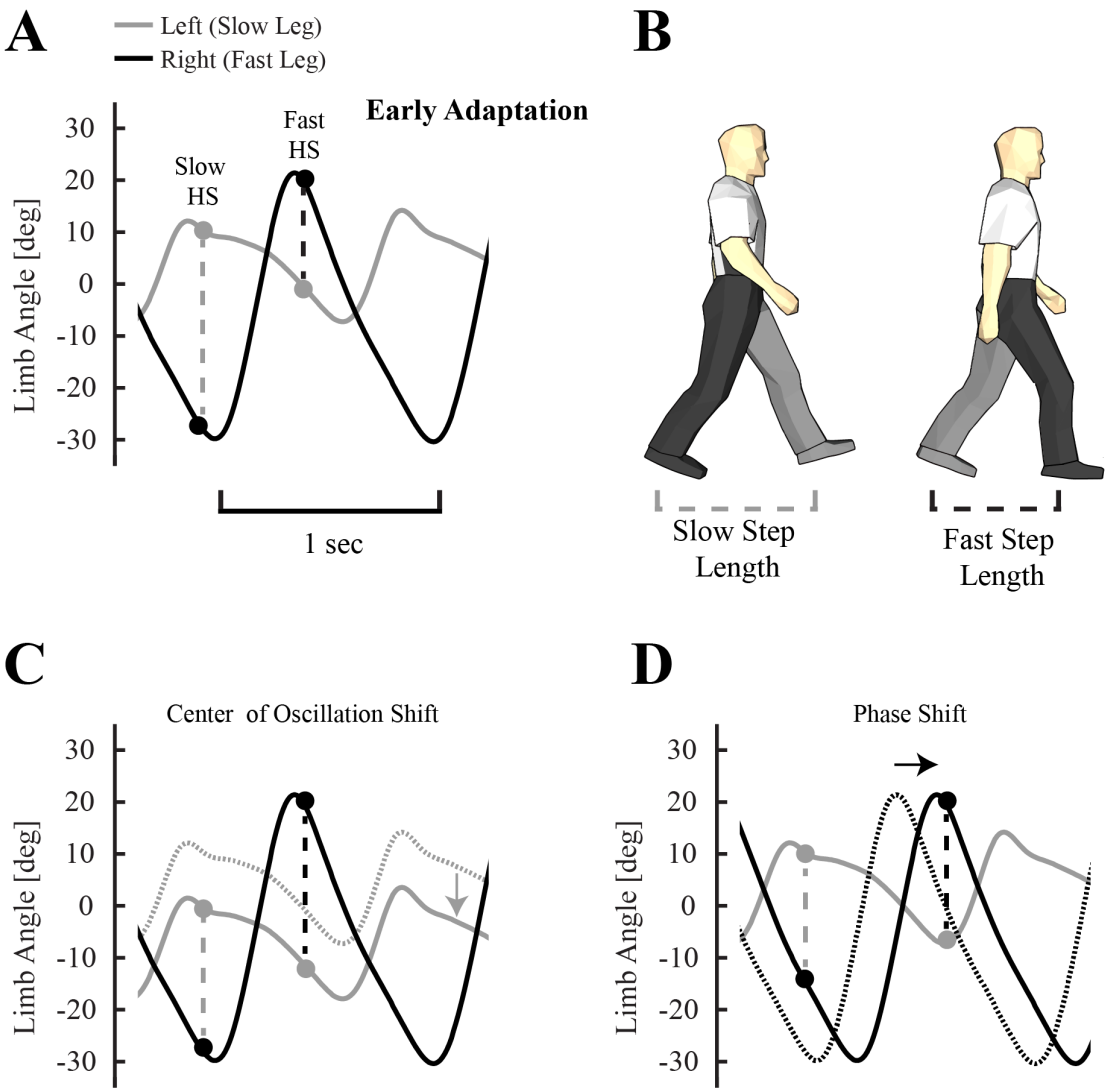

Figure 3.2 Early to late adaptation limb angle shifts toward symmetry using spatial and temporal strategies. **A**: Limb angle trajectories plotted over time for two cycles for a typical healthy individual in early adaptation. Positive angles indicate flexion (when the limb is in front of the trunk). "Slow leg" limb angle (in degrees) for the leg on the slow belt plotted in light grey and for the "fast leg" in black. Heel strikes (HS) are plotted as circles for each leg. **B**: Typical step lengths at the beginning of adaptation, with the fast leg step length starting off smaller than the slow leg step length. The difference in limb angles at HS (large dashed lines) is proportional to these step lengths. **C**: step symmetry (equal step lengths) can be achieved through shifting the limb angle curves vertically, a center of oscillation shift (a purely spatial change). **D**: step symmetry can also be achieved through changing the phase lag between the limb angles (moving the limb angle curves horizontally), which is a purely temporal change.

3.2.4.2 Walking Speed Perception

The walking speed perception task was designed to measure the ability of subjects to match the speed of their right leg to that of the left (set at a constant speed of 0.4 m/s). To assess performance, we recorded changes in right leg speed as the task was performed and quantified each subject's response to the task as the final speed of the right leg at the end of each 45 second trial.

3.2.5 Statistical Analysis

3.2.5.1 Sensory Assessments

Subjects performed the walking speed matching task at multiple time-points during post-adaptation, yet we expected the greatest sensory aftereffect (and less interference due to unlearning effects) to occur during early post-adaptation. As such, we compared performance on the speed matching task between groups during baseline and initial post-adaptation (i.e. the first performance of the speed matching task in post-adaptation) using student t-tests. The α level for significance was set at $p = 0.05$.

3.2.5.2 Motor Assessments

Baseline walking averages (last 10 strides of baseline walking) of step symmetry, phasing, and center of oscillation were first verified to be similar between the groups using student t-tests, and were subsequently subtracted from adaptation and post-adaptation data to normalize the data to baseline values. Given previous work showing that the cerebellum may be more involved in the acquisition phase of learning (Galea et al., 2011; Jayaram et al., 2012), rather than the absolute magnitude of motor learning, we split our analysis into these two parts: acquisition versus retention of the walking pattern. To determine changes in motor behavior throughout adaptation (acquisition of the new

walking pattern), separate two-way repeated-measures ANOVAs with between subjects factor GROUP (Cerebellar, Control) were used to compare changes in the average step symmetry, phasing, and center of oscillation difference between early adaptation (first 5 strides of adaptation) and late adaptation (last 30 strides of adaptation). To compare retention of the learned walking pattern (i.e. magnitude of learning), separate two-way repeated-measures ANOVAs with between subjects factor GROUP were performed to compare changes in the three motor parameters between the catch trial (first 2 strides of catch trial) and early post-adaptation (first 5 strides of post-adaptation). Post-hoc analysis was performed using the Bonferroni correction and the α level for significance was set at $p = 0.05$. The Greenhouse-Geisser correction was used as needed to correct for violations of Mauchly's test of sphericity.

3.2.5.3 Motor Behavior During Sensory Assessments

To understand the relationship between changes in the motor and sensory domains, we additionally analyzed subjects' motor behavior (in terms of step symmetry, phasing, and center of oscillation difference) while they performed the post-adaptation speed perception tasks. For each walking parameter, we performed a two-way repeated-measures ANOVA with within subjects factor TIME (time-points corresponded to the mean of the first 10 strides of each task performance; 6 total time-points) and between subjects factor GROUP. Post-hoc analysis was performed using the Bonferroni correction and the α level for significance was set at $p = 0.05$. The Greenhouse-Geisser correction was used as needed to correct for violations of Mauchly's test of sphericity. To determine the relationship between motor performance during walking and during the speed matching task, we additionally ran Pearson's correlations We additionally ran Pearson's

correlations for each motor parameter to compare performance at the end of adaptation and during the catch trial to performance during the post-adaptation speed matching task. We report the correlation coefficient, r, and set the α level for significance at $p = 0.05$.

3.3 Results

3.3.1 Speed Perception

We first assessed whether cerebellar patients and healthy controls had baseline differences in walking speed perception. Our t-test for baseline task performance showed no significant differences between the groups (Figure 3.3A; p = 0.413). Figure 3.3B shows group speed perception task responses at the six post-adaptation time-points. Note that baseline performance is subtracted out, so that zero represents baseline performance. Our t-test for the first post-adaptation time-point revealed a statistically significant difference between the groups (p = 0.004). In other words, while healthy controls demonstrated an initial sensory aftereffect in post-adaptation, cerebellar patients did not.

3.3.2 Motor Behavior

Group averages for step symmetry, phasing and center of oscillation difference (COD) are shown in Figures 3.4A, 3.4B, and 3.4C, respectively. Data is smoothed with running averages of three strides with the exception of catch trial and end adaptation averages, and each walking period (baseline, adaptation, post-adaptation) is truncated to the smallest number of strides across subjects. Data are shown as mean ± standard error of the mean (SEM). No baseline (tied-belt) differences in any parameter existed between cerebellar patients and healthy controls (phasing: p = 0.229; COD: p = 0.957; step

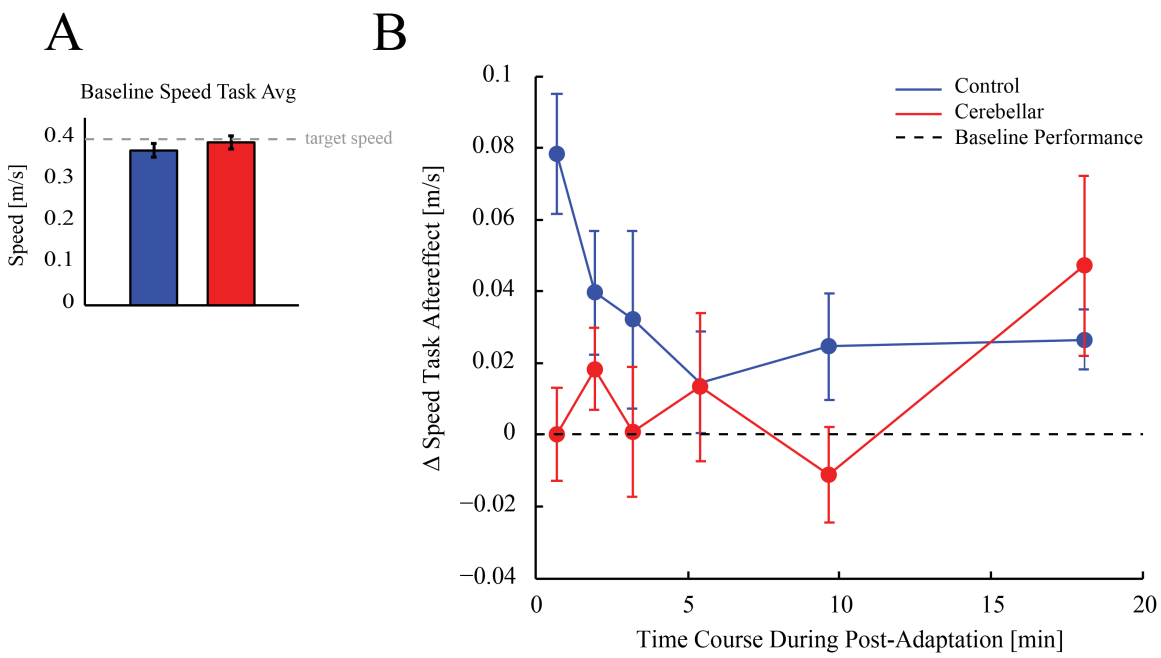

Figure 3.3 Baseline and post-adaptation speed matching task responses. Control group is shown in blue and cerebellar group in red. Error bars represent SEM. **A**: Baseline speed task averages (across all 3 baselines tasks, across groups) plotted in terms of absolute speed (m/s). Target (left leg) speed of 0.4 m/s shown as a grey dashed line. There were no differences found between groups ($p = 0.413$). Also, the control group ($p = 0.131$) and the cerebellar group ($p = 0.624$) were not significantly different from the target speed of 0.4 m/s, indicating both groups could perform the task very well. **B**: Baseline subtracted post-adaptation speed task group averages plotted as a function of time after the end of adaptation. The control group showed robust aftereffects that decayed over time while the cerebellar group did not show any aftereffects. Comparison of the initial post-adaptation task averages revealed a significant difference between groups ($p = 0.004$).

symmetry p = .701). As such, we subtracted mean baseline values from the data to normalize all data to baseline performance.

To determine differences in acquisition of the learned walking pattern, we compared changes in phasing, center of oscillation difference, and step symmetry between early and late adaptation. Our ANOVAs found significant effects of TIME in each parameter (phasing: $F(1,14) = 34.667$), $p < 0.001$; COD: $F(1,14) = 5.717$), $p = 0.030$; step symmetry: $F(1,14) = 28.196$), $p < 0.001$). However, neither parameter yielded significant effects of GROUP (phasing: $p = .243$; COD: $p = 0.967$; step symmetry: $p = 0.291$) or GROUPxTIME interactions ($p = 0.394$; $p = 0.337$; $p = 0.289$, respectively). These results indicate that the initial perturbation amount and level of adaptation did not differ between cerebellar patients and healthy controls in any parameter.

Analysis of the magnitude of learning (i.e. changes between the catch trial and early post-adaptation aftereffects), however, revealed more varied results. Our ANOVA for phasing revealed a significant main effect of TIME ($F(1,14) = 19.833$, $p = 0.001$) and an interaction of GROUPxTIME ($F(1,14) = 7.77$, $p = 0.015$), but no main effect of GROUP ($F(1,14) = 0.391$ $p = 0.542$). The interaction suggests that cerebellar patients had more forgetting in the temporal domain in the early post-adaptation. This may have been due to faster washout during the first post-adaptation speed-matching task. On the other hand, ANOVA for COD showed a significant main effect of GROUP ($F(1,14) = 7.192$, $p=0.018$), but no effect of TIME ($F(1,14) = 0.658$, $p = 0.431$) or GROUPxTIME interaction ($F(1,14) = 0.723$, $p = 0.409$). Similar to the COD result, ANOVA for step symmetry found a significant main effect of GROUP ($F(1,14) = 5.941$ $p = 0.029$) but no effect of TIME ($F(1,14) = 1.536$, $p = 0.236$) or GROUPxTIME interaction

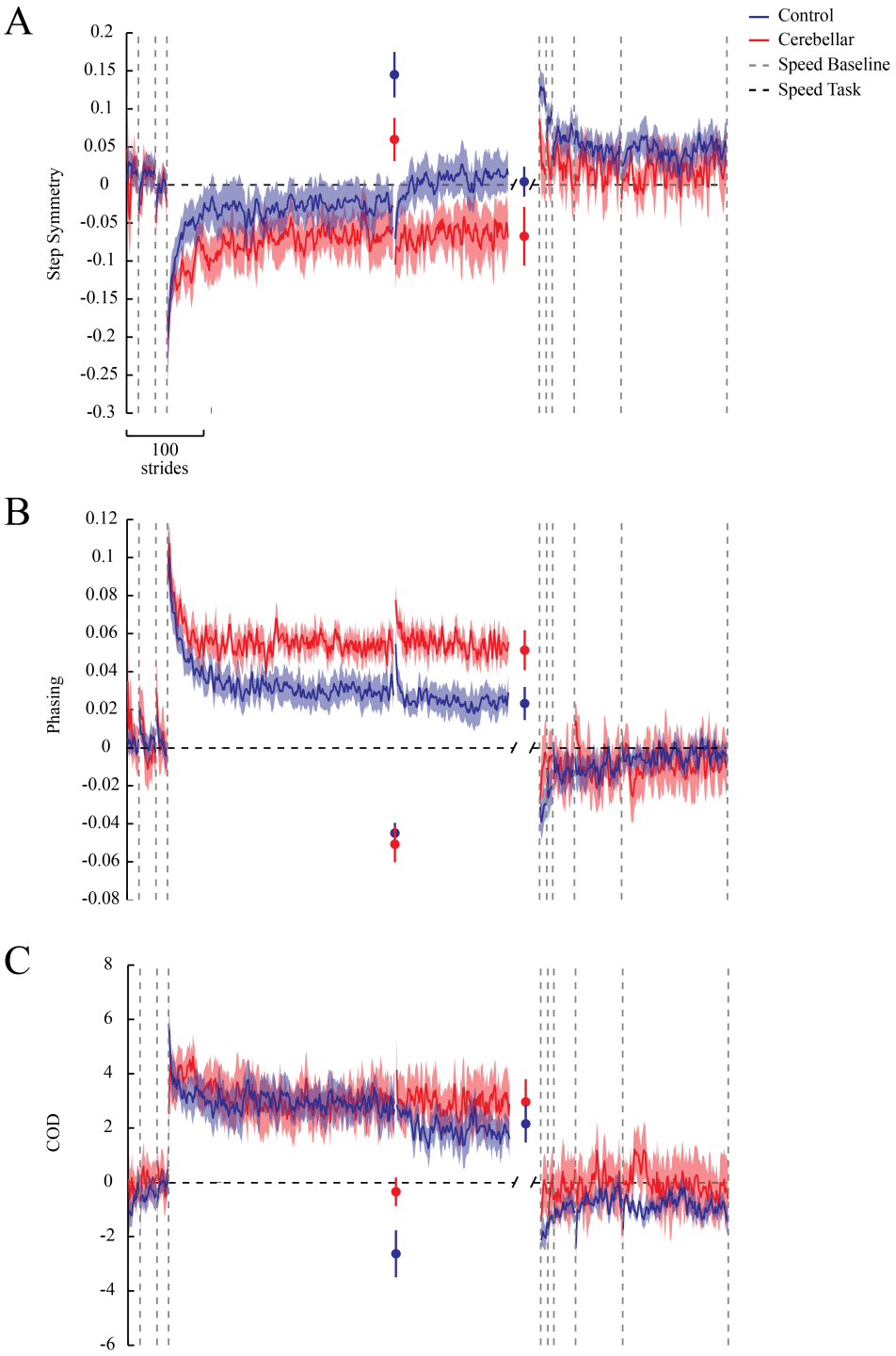

Figure 3.4 Group spatiotemporal kinematic performance for phasing, center of oscillation difference (COD) and step symmetry. Control group shown in blue and Cerebellar group in red. Curves are smoothed with a running average of 3 strides and all data is baseline subtracted. Data truncated for every block in the experiment for alignment. Shaded regions represent standard error of the mean (SEM). Grey dashed lines indicate where the walking speed matching tasks took place (~15 strides). Black dashed

line represents perfect symmetry (0). **A**: Step symmetry ANOVA for acquisition only showed a main effect of TIME ($F(1,14) = 28.196$), $p < 0.001$). The magnitude of learning ANOVA also only showed a main effect of GROUP ($F(1,14) = 5.941$ $p = 0.029$), indicating a significant reduction in learning by the patients in step symmetry. **B**: The phasing RM ANOVA for comparing acquisition of the walking pattern only revealed a main effect of TIME ($F(1,14) = 34.667$), $p < 0.001$). The ANOVA comparing magnitude of learning similarly only showed a main effect of TIME ($F(1,14) = 19.833$, $p = 0.001$). **C**: COD ANOVA comparing acquisition only revealed a main effect of TIME ($F(1,14) = 5.717$), $p = 0.030$). The magnitude of learning ANOVA however, showed a main effect of GROUP ($F(1,14) = 7.192$, $p = 0.018$) but not effects of TIME or interaction, indicating a reduction in learning for COD of patients compared to controls.

($F(1,14) = 0.022$, $p = 0.884$). Taken together, these results indicate that cerebellar damage primarily led to deficits in the magnitude of learning in the spatial and spatiotemporal domains, but not in the temporal domain (although they may have had quicker forgetting in the temporal domain). Further, they suggest that the deficits in step symmetry learning appear to be driven primarily by deficits in spatial learning, rather than temporal.

3.3.3 Speed Perception Motor Results

Figure 3.5 shows average group performance for the three motor parameters, step symmetry (Figure 3.5A), phasing (Figure 3.5B), and COD (Figure 3.5C), during the post-adaptation speed perception tasks. We qualitatively observe that motor behavior of all three parameters during the speed perception task parallels that of the magnitude of learning during adaptation. Specifically, it appears that cerebellar patients exhibit differences in step symmetry compared with healthy controls. Quantitatively, our ANOVA for step symmetry found a significant main effect of TIME ($F(5,70) = 4.982$, $p = 0.001$), and a GROUPxTIME interaction ($F(5,70) = 3.209$, $p = 0.011$), but no effect of GROUP ($p = 0.302$). Post-hoc analysis of step symmetry at each time-point revealed a significant difference between groups during the first post-adaptation task ($p = 0.02$) and a trend towards significance during the second task ($p = 0.091$), but no significant differences on subsequent time-points. This suggests a difference in decay rate in step symmetry during the post-adaptation tasks. For COD, ANOVA did not reveal any statistically significant results (TIME: $p = 0.140$; GROUP: $p = 0.197$; GROUPxTIME: $p = 0.117$). Lastly, our ANOVA for phasing found a significant main effect of TIME ($F(5,70) = 9.648$, $p < 0.001$), but no effect of GROUP ($p=0.335$) or GROUPxTIME interaction ($p = 0.281$). These results demonstrate that while performing the speed

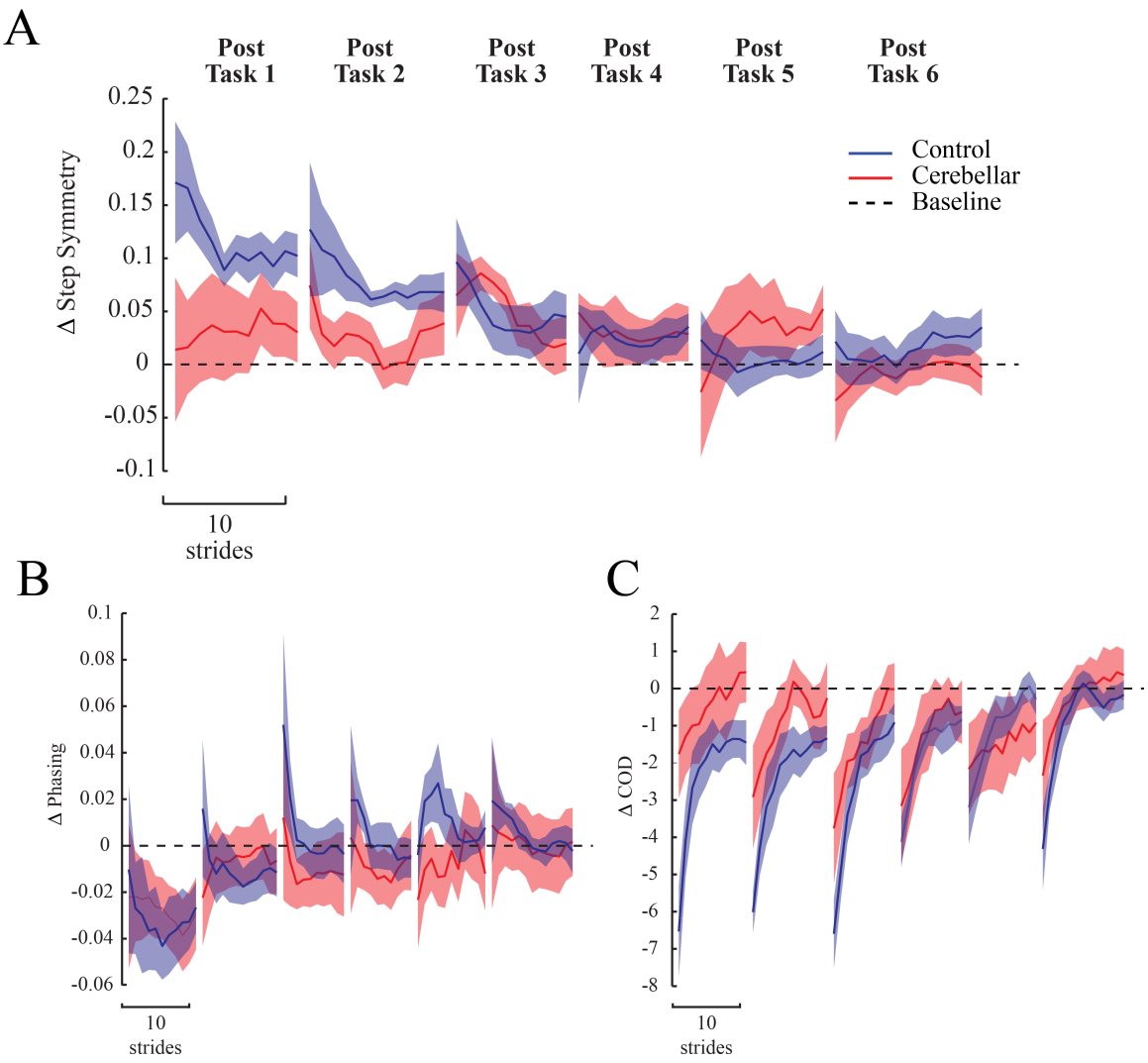

Figure 3.5 Group spatiotemporal kinematic performance for step symmetry (A), phasing (B) and center of oscillation difference (C) during the six post-adaptation speed matching tasks. Curves are smoothed with a running average of 3 strides and all data is baseline subtracted. Data truncated for every post-task for alignment. Shaded regions represent SEM. Baseline performance indicated by a black dashed line. **A**: The step symmetry ANOVA showed a main effect of TIME ($F(5,70) = 4.982$, $p = 0.001$), and an interaction of GROUPxTIME ($F(5,70) = 3.209$, $p = 0.011$) but not effect of GROUP ($F(1,14) = 1.150$, $p = 0.302$). This suggests that post task behavior step symmetry showed aftereffects, which decayed over time for the control group but not the cerebellar group. **B**: In phasing, we found a significant effect only of TIME ($F(5,70) = 9.648$, $p < 0.001$). **C**: The COD ANOVA did not reveal any significant effects.

matching task after adaptation, healthy controls exhibited motor aftereffects in step symmetry which decayed over time, yet cerebellar patients demonstrated impaired motor aftereffects. This further suggests that performance of the speed matching task may be linked to the global spatiotemporal component of walking (i.e. step symmetry). In addition, we qualitatively observe that the effect on step symmetry may have been driven primarily by a non-significant difference in spatial coordination, rather than temporal.

3.3.3.1 Spatial components of adaptation and speed task linked to perceptual aftereffects

To further investigate what was driving changes in step symmetry, we conducted Pearson's correlations, which indicate the extent to which subjects attempted to recreate their adapted state during the post-adaptation speed matching tasks. We specifically compared performance between the last 30 strides of adaptation and the last 5 strides of the first post-adaptation speed matching task. The results of these correlations are shown in Figures 3.6A (step symmetry), 3.6B (phasing), and 3.6C (COD). We found a significant correlation between the end of adaptation and the speed matching task for COD ($r = 0.74$, $p < 0.01$), but no correlations for phasing ($r = 0.01$, $p = 0.98$) or step symmetry ($r = 0.287$, $p = 0.30$). One cerebellar patient was removed from the analysis of step symmetry whose data were greater than two standard deviations away from the group mean. This was the only outlier data point for any of our analyses. We additionally compared the catch trial magnitude of each parameter to performance during the first speed matching task, and found similar results, shown in Figures 3.6D-F (step symmetry, phasing and COD, respectively). Specifically, there was a significant correlation for COD ($r = -0.54$, $p < 0.05$), but no correlations for phasing ($r = -0.13$, $p = 0.96$) or step symmetry ($r = 0.38$, $p = 0.15$). This evidence suggests that when performing the speed

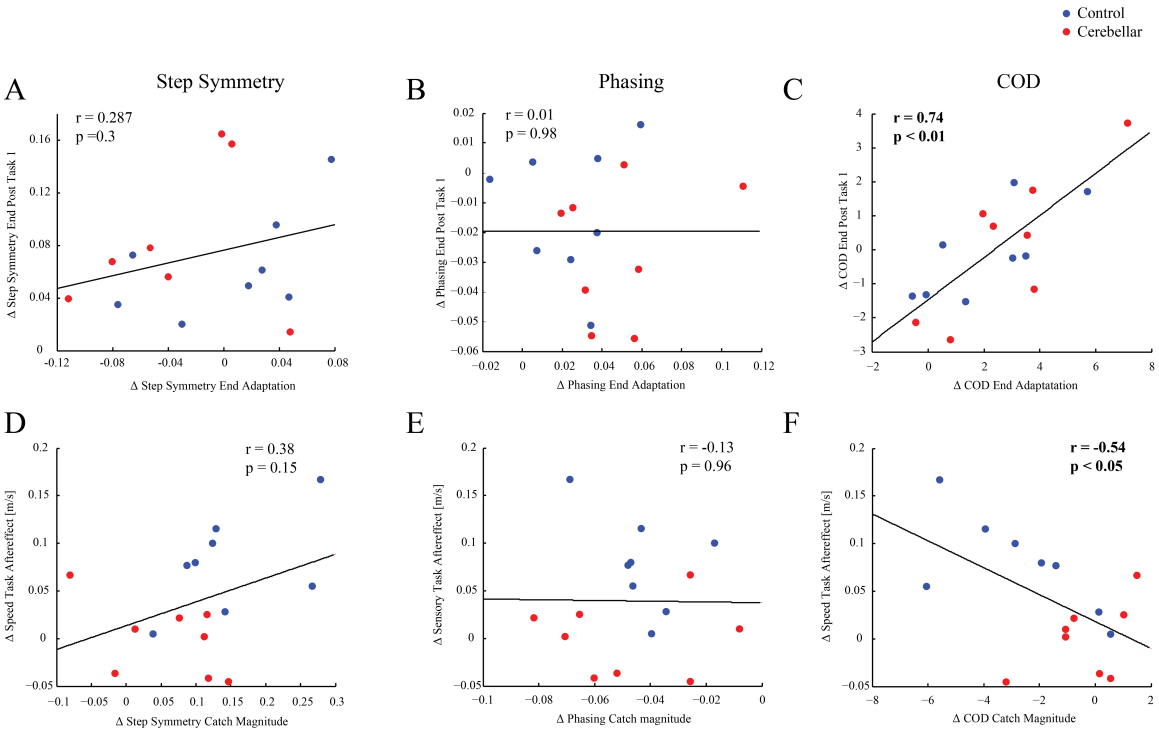

Figure 3.6 Correlations showing how subjects achieve perceptual symmetry and relationship to magnitude of learning. Control subjects are shown in blue and cerebellar subjects are shown in red. Each circle is data for an individual subject. **A-C**: Correlations relating what subjects achieved in the motor domain for step symmetry (A), center of phasing (B), and center of oscillation difference (C) at the end of the first post-adaptation speed task (last 5 strides) and what subjects correspondingly achieved at the end of adaptation (last 30 strides) for the same parameter. Only COD showed a significant correlation (Pearson correlation coefficients on figures). **D-F**: Correlations relating the magnitude of learning (catch trial average) in each parameter with the amount of initial perceptual speed aftereffect (post-task 1). Again, only COD showed a significant correlation.

matching task, subjects as a whole attempted to recreate the spatial component of their adapted state. Further, at least in the spatial domain, the amount of learning could predict the amount of perceptual speed aftereffects.

3.4 Discussion

The purpose of this study was to determine the role of the cerebellum in the motor and perceptual components of split-belt walking adaptation. We found that patients with cerebellar damage have intact magnitude of learning in a temporal component of walking but deficits in the spatial domain. Alongside this impaired spatial learning, patients exhibited deficits in the recalibration of leg speed perception after adaptation. Overall, these results suggest that the cerebellum is an important brain structure for motor and perceptual sensory changes, which occur as a result of locomotor adaptation.

Our current findings in healthy, older adults confirmed previous results demonstrating that split-belt walking leads to recalibration of leg speed perception in healthy, young adults (Jensen et al., 1998). However, although the control group showed robust perceptual aftereffects, our cerebellar patients did not. Given that cerebellar patients had no impairment in leg speed perception at baseline, we attribute these results to a lack of perceptual recalibration during the adaptation phase. Our analysis additionally suggests that both healthy and cerebellar subjects attempted to achieve perceptual speed symmetry (i.e. what "felt" like the legs were moving the same speed) by recreating the spatial, but not temporal, component of their adapted walking pattern. Further, the amount of learning in the spatial domain (as seen in the catch trial) predicted the amount of perceptual speed aftereffects on a subject-to-subject basis. This evidence suggests that the recalibration and retention of speed perception are likely more

dependent on the spatial components of motor adaptation. However, while there appears to be a clear link between perceptual recalibration deficits and spatial motor learning deficits in cerebellar patients, it is not yet known whether changes in the motor domain drive sensory changes or if they are independent processes, which are both reliant on the cerebellum.

Our results are consistent with the idea that the cerebellum houses and recalibrates a forward model that predicts the sensory consequences of movement. First, the lack of perceptual aftereffects in our cerebellar group allows us to reject our alternative hypothesis that perceptual recalibration after split-belt adaptation is due to separate learning mechanisms (e.g. use-dependent plasticity). Instead, it appears that this sensory recalibration is directly related to the cerebellar-dependent, error-driven motor adaptation process. Previous studies show that cerebellar patients exhibit changes in perceived hand position after reaching adaptation, but these sensory aftereffects are smaller compared to healthy controls (Criscimagna-Hemminger et al., 2010; Izawa et al., 2012). However, Henriques and colleagues (2014) suggest that this ability of cerebellar patients to recalibrate perceived hand position is driven by changes in hand proprioception due to a visual-proprioceptive cross-sensory signal experienced in reaching adaptation. Our result that cerebellar patients do not exhibit sensory aftereffects, then, may be explained by the lack of such a salient cross-sensory error signal in walking adaptation, suggesting that intact cerebellar function is necessary to produce this type of sensory recalibration.

We were surprised to find significant differences in the spatial and temporal components of walking adaptation. One possible explanation of this result is the cerebellum may preferentially affect recalibration of spatial components of a forward

model during walking. The link between the cerebellum and the spatial components of walking may be explained by the vast amounts of sensory information available to the cerebellum, such as foot contact (Apps & Lidierth, 1989) and limb angle (Bosco & Poppele, 2001). On the other hand, the temporal components of walking may be more closely tied to structures in the spinal cord, brainstem centers, and/or the motor cortex. The spinal cord, for example, plays an important role in locomotor control and has been modeled in a variety of animals as providing important signals of timing during walking through central pattern generators (Arshavsky et al., 1997; Grillner et al., 2000; Kiehn, 2006; McCrimmon et al., 2000; Rybak et al., 2006a, 2006b; Selverston, 1993; Zelenin et al., 2000). In contrast to the present finding that adaptation of temporal components is preserved in cerebellar patients, a previous study from our lab showed that cerebellar patients were able to adapt to a split-belt treadmill in the temporal domain, yet the magnitude of temporal aftereffects were smaller than that of healthy controls (Morton & Bastian, 2006). Possible explanations for this discrepancy in the results are differences in the size of the perturbation and the duration of adaptation. Compared to the previous study, here we used a slightly smaller perturbation (split-belt speeds of 0.4/0.8 m/s, compared to 0.5/1.0 m/s in the previous study) and a longer duration (15 min vs. 10 min). Our smaller perturbation may have facilitated greater motor learning, as learning from smaller errors has been suggested to create a better environment for motor learning in cerebellar patients (Criscimagna-Hemminger et al., 2010; Izawa et al., 2012). Alternatively, it is possible that patients used an explicit spatial strategy (e.g. consciously moving the right leg farther) to compensate for the spatial perturbation, creating a similar motor pattern to that of controls. However, such a cognitive strategy may have

circumvented the adaptation processes, which normally lead to recalibration of a forward model, demonstrated by reduced catch trial and initial aftereffect magnitudes.

We have shown that cerebellar function is important for achieving perceptual speed aftereffects after split-belt adaptation. However, it is hard to dissociate whether the cerebellum is directly involved in the perceptual recalibration itself or whether deficits in motor recalibration subsequently cause downstream deficits in perceptual adaptation processes. Several neurophysiological studies provide evidence that the cerebellum may control movement velocity, specifically suggesting that Purkinje cell discharge in the cerebellum can be tuned to a specific direction–speed combination during visually guided reaching tasks (Coltz et al., 1999; Johnson & Ebner, 2000; Mano & Yamamoto, 1980; Marple-Horvat & Stein, 1990; Miles et al., 2006). However, there is not sufficient evidence to connect the cerebellum's *control* of movement velocity with its influence in velocity *perception.* Instead, we believe the cerebellum is more likely part of a network whose influence on motor commands also affects perception downstream. Supporting this notion, a recent study used fMRI to measure functional changes before and after subjects adapted to an abrupt force-field perturbation, and showed that changes in connectivity between right cerebellar cortex and frontal motor areas (motor cortex and supplementary motor area) depended only on motor learning, connectivity between secondary somatosensory cortex and other frontal motor areas (ventral premotor and supplementary motor area) were more dependent on sensory changes, and connectivity between the cerebellum and the superior parietal lobule (SPL) were equally dependent on motor and sensory changes (Vahdat et al., 2011). Interestingly, the SPL is thought to be involved with spatial orientation. Overall, this evidence provides insight into the spatial

deficits we observed in our cerebellar patients' motor behavior as well as the link between their motor and sensory recalibration deficits.

We have shown that patients with cerebellar damage exhibit deficits in the recalibration of leg speed perception, which normally occurs after locomotor adaptation in healthy people. Further, this sensory recalibration impairment appears to be linked to a deficit in the spatial components of motor adaptation. To our knowledge, this is the first study to show a clear preservation of the magnitude of learning of a temporal component of motor adaptation in cerebellar patients. Though it has yet to be determined whether perceptual recalibration occurs in the cerebellum or is more reliant on a larger network of brain structures, we conclude that deficits in both spatial adaptation and perceptual recalibration are undoubtedly linked to cerebellar function.

CHAPTER 4

Effect of Error Size on Motor and Perceptual Recalibration

4.1 Introduction

Sensorimotor adaptation is essential for counteracting the constant uncertainties we face in our environment and with our bodies as we move about. When making a movement, our nervous system predicts the sensory consequences of the action and, through sensory feedback, can assess how well we executed our intended motor command (Kawato, 1999; Tseng et al., 2007). The difference between the actual and desired state - the sensorimotor prediction error – is minimized throughout motor adaptation and in the process a recalibration to the motor system occurs but changes to perception can also occur simultaneously. These errors can arise from two main sources: externally, from the environment or a device; or internally, from the body. It is thought that smaller errors, more like those naturally encountered, are more likely to be attributed internally and therefore generalize better to other motor movements (Berniker & Kording, 2008). We previously showed that when learning a new walking pattern on a split-belt treadmill, small, predictable errors lead to greater generalization to over-ground walking compared to large errors (Torres-Oviedo & Bastian, 2012). These results suggest that the small errors experienced from a gradually-induced perturbation may be attributed to internal factors and consequently lead to greater motor recalibration and generalization compared to the large errors from an abrupt perturbation.

Along these lines, it is thought that learning a movement from a gradual perturbation results in a more stable motor memory (i.e. the motor pattern is retained longer and decays more slowly) (Huang & Shadmehr, 2009). Studies of reaching adaptation have shown that gradual perturbations can lead to larger motor aftereffects immediately after learning (Kagerer et al., 1997) and greater retention 24 hours later (Klassen et al., 2005) compared to abrupt perturbations. Additionally, one recent study (Mattar et al., 2013) demonstrated a trend toward larger perceptual aftereffects for a force-field perturbation that was introduced gradually versus abruptly but this result was only anecdotal. In contrast, our aforementioned split-belt treadmill study (Torres-Oviedo & Bastian, 2012) showed that abrupt, rather than gradual, perturbations resulted in larger aftereffects and a more recent study (Patrick et al., 2014) found no difference between abrupt and gradual split-belt perturbations. Thus, it is unclear how abrupt and gradual locomotor perturbations might differentially effect motor aftereffects.

In addition to learning from a gradual perturbation, other motor skill learning studies have shown that *overlearning* (i.e.additional training that has little effect on performance after a high level has been reached) can also lead to more retention shortly after (Melnick, 1971; Melnick et al., 1972; Schendel & Hagman, 1982, 1991) or even some time (e.g. 24hrs) after training (Craig et al., 1972; Driskell et al., 1992; Postman, 1962; Rohrer et al., 2005). One study showed increased retention (after 5 min and 24 hours) in a force-field reaching task for groups that experienced longer adaptation periods (Joiner & Smith, 2008). Here we examine overlearning in the context of split-belt adaptation to determine whether overlearning in split-belt adaptation will result in larger motor and leg speed perception aftereffects.

It is thought that motor adaptation can also lead to a recalibration of sensory perception. Studies in reaching adaptation have shown that estimates of hand position are reliably recalibrated after visuomotor (Cressman & Henriques, 2009; Salomonczyk et al., 2011, 2012) and force-field reaching adaptation (Haith et al., 2008; Mattar et al., 2013; Ostry et al., 2010). In walking, it has been shown that there can also be changes to perception of leg speed after (at one time point) walking with an *abrupt* split-belt perturbation where one leg is suddenly driven to walk three times as fast as the other (Jensen et al., 1998). Though that particular study did not show how the motor system played a role in the perceptual changes, we believe that the changes in speed perception are in someway linked to the amount and type of learning in the motor domain. In this study we aimed to extend the work from Jensen by investigating the role of motor learning in modulating leg speed perception after split-belt adaptation and showing how this perception decays over an extended period of time.

Here we investigated how gradual, abrupt and extended abrupt split-belt treadmill perturbations affect both motor and sensory recalibration. In experiment 1, we asked how healthy adults adapt to and retain a split-belt walking pattern under various perturbation sizes and doses. In experiment 2, we investigated how these perturbation conditions might differentially affect perception of leg speed. We hypothesized that gradual adaptation, causing small movement errors more likely to be attributed to internal factors, would lead to the greatest recalibration in both the motor and sensory domains.

4.2 Materials and Methods

4.2.1 Subjects

Forty-eight healthy, right hand and right leg dominant, volunteers (12 males and 36 females; mean age, 23.6 +/- 3.2 years) participated in this study. All subjects were prescreened for self-reported hand and leg dominance, neurological, and/or motor dysfunction. The protocols were approved by the Johns Hopkins Institutional Review Board and all participants provided written informed consent before testing.

4.2.2 Experimental Setup

Split-belt treadmill walking. Split-belt walking was studied using a custom-built treadmill (Woodway, Waukesha, WI). Speed commands for each belt were sent to the treadmill through either a custom MATLAB (The MathWorks, Natick, MA) program or a custom Python program in the Vizard (WorldViz, California USA) development environment. Subjects wore a safety harness which did not support their body weight and were positioned in the middle of the treadmill with one leg on each belt. A wooden divider separated the two treadmill belts to ensure each leg stayed on its respective belt.

Optotrak motion analysis. Kinematic data were collected at 100 Hz using Optotrak (Northern Digital, Waterloo, ON, Canada). Bilateral infrared-emitting markers were placed over the toe (fifth metatarsal head), ankle (lateral malleolus), knee (lateral femoral epicondyle), hip (greater trochanter), pelvis (iliac crest), and shoulder (acromion process).

4.2.3 Experimental Protocols

4.2.3.1 Experiment 1 – Motor Performance

In Experiment 1, we investigated the differences in motor adaptation and retention with three separate types of perturbation schedules. The general paradigm for Experiment

1 is shown in Figure 4.1A. All subjects completed a *baseline period* in which they walked with both belts at a *slow speed* (.5 m/s) for three minutes. In the subsequent *adaptation period*, each subject was randomly assigned to one of three groups, each with a different type of split-belt perturbation (see Figures 4.1C-E for perturbation types). The Short Abrupt group (Figure 4.1C) experienced an abrupt perturbation in treadmill belt speed such that the left belt moved at 0.5 m/s and the right belt moved at 1.5 m/s. These belt speeds were maintained for 15 minutes. The Extended Abrupt group (Figure 4.1E) was to determine how overlearning the split-belt walking pattern might influence motor or sensory retention. Participants in this group experienced the same abrupt perturbation as the Short Abrupt group, but it persisted for 25 minutes, rather than 15. The Gradual group (Figure 4.1D) began walking with both belts moving at 0.5 m/s, and the right belt gradually increased speed at a rate of 0.1 m/s per minute for 10 minutes until it reached a speed of 1.5 m/s. Subjects then walked for 5 additional minutes at this 0.5:1.5 m/s belt speed ratio. To probe the magnitude of learning during adaptation, all subjects experienced a *catch trial* after 10 minutes of adaptation during which they walked for 10 seconds with tied belts (i.e. both belts moving at 0.5 m/s). After the *adaptation period*, subjects in all groups experienced a *post-adaptation* period during which both treadmill belts moved at 0.5 m/s in order to assess retention of the newly learned walking pattern.

4.2.3.2 Experiment 2 – Motor Performance and Leg Speed Perception

In Experiment 2, we examined the effects of the perturbation types from Experiment 1 on leg speed perception (Figure 4.1B). Like Experiment 1, all subjects experienced *baseline, adaptation, catch, and post-adaptation periods*, but were additionally asked to perform a speed matching task three times briefly during the

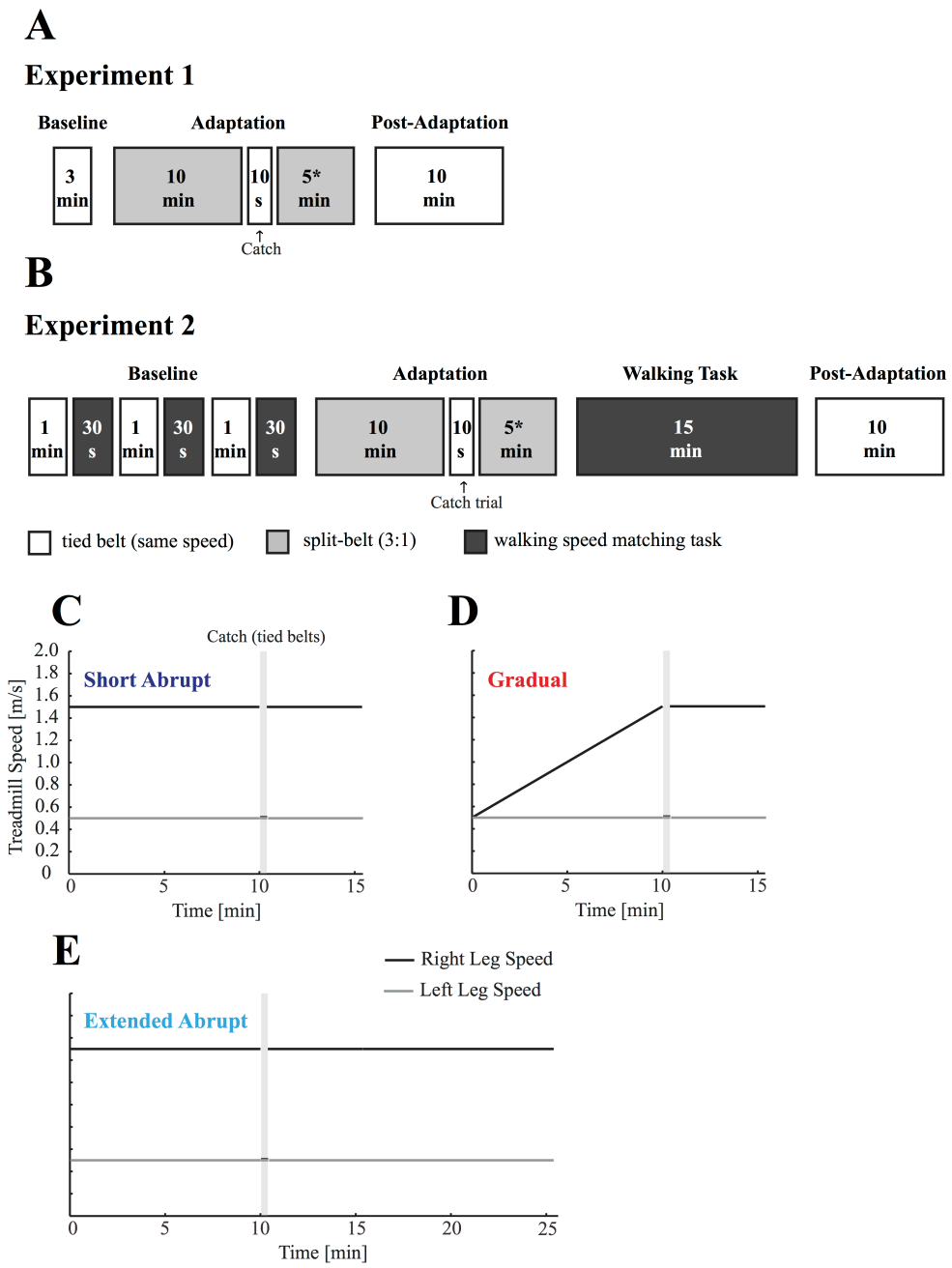

Figure 4.1 Experiment 1 and 2 general paradigms and perturbation schedules. **A**: in all groups, subjects experienced a continuous baseline walking period of 3 min where both belts were tied at .5 m/s. This was followed by the adaptation period where each subject received one of the split-belt perturbations (right leg fast) whose speeds are shown in parts C-E. Ten minutes into adaptation all subjects experienced a catch trial of 10 s where both belts were returned to the baseline speeds of .5 m/s. Subjects were then readapted accordingly for 5 minutes in all groups except the Extended Abrupt group (15 min). Finally, all subjects experienced the same post-adaptation period where both belts

returned to .5 m/s for 10 minutes. **B**: the basic walking adaptation paradigm for experiment 2 is the same as experiment 1 except all subjects performed three baseline speed matching tasks and 1 post-adaptation speed matching task. In the baseline period, subjects alternated between 1 minute of baseline walking (.5 m/s) and a 30 second speed matching task, for a total of 3 pairs. As in experiment 1, each subject experienced one of the perturbations described in parts C-E during the adaptation portion. Following, all subjects performed a continuous 15 minute speed matching task. At the start of each task the left belt was maintained at .5 m/s and the subject controlled the right belt speed and attempted to match their left leg speed. After the post-adaptation task all subjects experienced the post-adaptation walking period where both belts returned to .5 m/s. C-E: Left (grey) and right (black) belt speed time course for all perturbation types. In all cases, a catch trial where both belts returned to .5 m/s was administered for 10 sec, 10 minutes into adaptation. **C**: Short Abrupt group: the left and right belt speeds were maintained at .5 m/s and 1.5 m/s, respectively for 15 min total. **D**: Gradual group*:* Both belt speeds started tied at .5 m/s and the right belt speed was increased gradually to 1.5 m/s over the course of 10 minutes and then remained at 1.5 m/s for an additional 5 minutes. The left belt speed was maintained at .5 m/s for the total duration of 15 minutes. **E**: Extended Abrupt group: The left and right belt speeds were maintained at .5 m/s and 1.5 m/s, respectively for 25 min total.

baseline period, and continuously for 15 minutes in between the *adaptation* and *post-adaptation periods*.

4.2.3.3 Speed Matching Task

Leg speed perception was assessed via a novel leg speed matching task, similar to Jensen et al., 1998. The experimental setup is shown in Figure 4.2. Using the psychophysical method of adjustment, subjects were asked to manually adjust the right belt speed while walking to match that of the left belt speed (held constant). Subjects were positioned on the treadmill and instructed to place their left hand on a hand rail in front of the treadmill and their right hand on a small keypad. Vision of the legs was obstructed via an opaque drape, and auditory cues of speed from the treadmill motors were cancelled via headphones playing white noise. Initially, the left leg was driven to walk at a constant speed of 0.5 m/s, while the right leg was not moving. Subjects were instructed to press up or down arrows on the keypad in front of them to adjust the speed of the *right* leg until they perceived it to match the speed of the left leg (reference leg). The reference leg speed was always 0.5 m/s to avoid introducing a declarative memory component to the task of remembering the reference leg speed. Subjects were given 30 seconds to complete the task each time during baseline and 15 minutes to complete the task during post-adaptation, and were given feedback on the amount of time remaining via a television monitor in front of the treadmill. In contrast to the discrete, 30 second samples of speed matching performance taken during baseline, subjects were allotted an extended period of time to complete the task during post-adaptation in order to assess whether any sensory aftereffects of learning decay over time. While the right leg was within the range 0.0 - 0.45 m/s, keypresses resulted in speed increments of either .05,

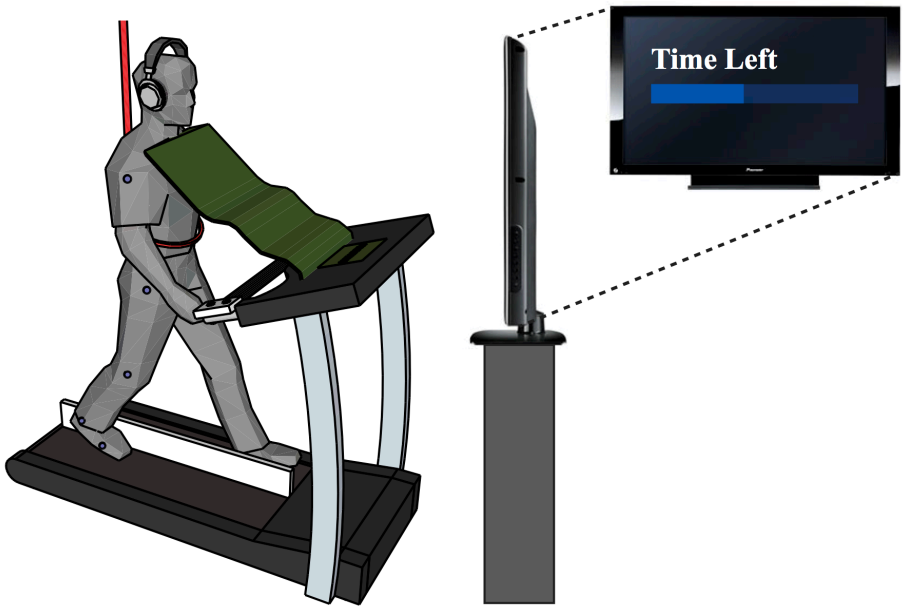

Figure 4.2 Diagram of subject performing the speed matching task. Subjects walked on a split-belt belt treadmill and were oriented with one leg on each belt, separated by a divider. A safety harness was secured around the waist and attached to the ceiling. Headphones playing white noise were worn by the subject to cancel any auditory cues. A flexible drape was worn and used to block vision of the legs. The keypad used to change the speed of the right belt was located off to the right and secured to the treadmill handle bar. IR led markers (6 on each side) were placed on specific anatomical locations on the subject's sides to track movements. Subjects faced a television screen that showed a progress bar indicating the time remaining for the task.

.055, or .065 m/s (these increments were changed each time the task was performed so subjects were unable to simply count the number of keypresses needed to reach the target speed). Once the speed passed 0.45 m/s, key presses resulted in a smaller change in speed, .005 m/s, to allow for fine control of speed as the right leg approached the target speed.

4.2.4 Data Analysis

4.2.4.1 Motor

In both experiments, our primary measure of motor performance was step symmetry, defined as the normalized difference between both step lengths, which has previously been shown to adapt and show robust aftereffects from split-belt walking (Reisman et al., 2005). This measure, step symmetry, is calculated using step lengths, where each step length was the anterior-posterior distance between the ankle marker of each leg at heel strike of the leading leg; fast step length refers to the step length measured at fast-leg (right leg) heel strike, and slow step length refers to the step length at slow-leg (left leg) heel strike. Step symmetry was calculated (Malone & Bastian, 2010) as the difference in slow step length subtracted from the fast, divided by their sum to allow for comparisons across subjects who might take different-sized steps and have different leg lengths. A value of 0 indicates symmetry. We then calculated the magnitude of step symmetry for each pair of steps throughout the experiment (Reisman et al., 2005). Step symmetry is typically plotted for each stride, which consists of two steps.

4.2.4.2 Leg Speed Perception

In Experiment 2, the walking speed perception task was carried out to measure the ability of subjects to match the speed of their right leg to that of their left (set at a constant speed of 0.5 m/s). To assess performance, we recorded changes in right leg speed as the task was performed. For baseline speed tasks, we quantified each subject's response to the task as the final speed of the right leg at the end of each 30 second trial. For the post-adaptation speed task we quantified the response as the *peak speed* achieved within the first 2 minutes of performing the task.

4.2.5 Statistical Analysis

4.2.5.1 Motor Performance

For both experiments, step symmetry was calculated at specific time-points throughout each experiment: baseline (last 10 strides of baseline walking), Catch trial (first 3 strides of catch trial), late adaptation (last 30 strides), early post-adaptation (first 5 strides of post-adaptation), and late post-adaptation (last 30 strides). The rate of unlearning was also calculated as the average of the first (baseline subtracted) 150 strides of post-adaptation. One-way ANOVAs were performed to compare baseline walking averages and unlearning rates. Two-way repeated measures ANOVAs on baseline subtracted step symmetry data for the catch, late adaptation, early post and late-post time points with between subjects factors GROUP and within subjects factor TIME were performed to compare changes to acquisition and magnitude of motor learning. For our supplementary analysis relating motor behavior during the end of adaptation and during the post-adaptation task we used a two-way repeated measures ANOVA with between subjects factor GROUP and within subjects factor TIME (end adaptation and peak task

response) for parameters step length and step time. Post-hoc analysis was performed using the Bonferroni correction. The Greenhouse-Geisser correction was used as needed to correct for violations of Mauchly's test of sphericity. To investigate the specific motor behavior subjects employed while performing the speed matching task, we additionally decomposed motor behavior into individual step lengths and step times (i.e. the time between consecutive heel strikes, see Finley et al., 2013) and conducted Pearson correlations on these parameters to determine the relation between motor behavior at the end of adaptation and during the peak speed matching task response. The α level was set at $p = 0.05$ as a measure of significance for all statistical analyses. All analyses were completed with SPSS (IBM Corp, Armonk, NY) statistics software.

4.2.5.2 Leg Speed Perception

Unlike our motor performance data, we found speed matching response aftereffect data to be non-normally distributed as indicated by a Shapiro-Wilk test ($W = 0.732$, $p < 0.001$); thus, we used Kruskal-Wallis H tests to statically compare both baseline and post-adaptation speed aftereffect responses. Post hoc analyses were performed using Mann-Whitney U-tests. We also used Wilcoxon signed-rank tests to test for significant aftereffects (baseline and peak speed aftereffects) for each group. For these analyses, the α level was set at $p = 0.05$.

4.3 Results

4.3.1 Experiment 1

Average baseline step symmetry was not statistically different between groups ($F(2,23) = 1.684$, $p = 0.21$). Therefore, we subtracted the average values of symmetry during baseline (tied belt) walking from all data.

In general, we found that motor learning and retention were not significantly different across groups. Single subject step symmetry data for typical Short Abrupt (left) and Gradual (right) group subjects are shown in Figure 4.3A. The Short Abrupt group subject is able to reduce the step symmetry error throughout adaptation and shows learning as exhibited by the catch trial and post-adaptation. The Gradual group subject is able to maintain symmetry with the incremental perturbation but still shows aftereffects during the catch and post-adaptation as well. Group step symmetry adaptation data is shown in Figure 4.4A. Since adaptation curves are truncated to the smallest number of strides across subjects, averages for end of adaptation (last 30 strides) are shown in the inset bar graph (Figure 4.4A). Our two-way repeated measures ANOVA showed a significant effect of TIME (for catch, late adapt, early post and late post averages) ($F(3,63) = 90.664$, $p < 0.001$) but no significant differences for GROUP ($F(2,21) = 0.070$, $p = 0.932$) or interaction of GROUP x TIME ($F(6,63) = 0.626$, $p = 0.616$). For clarity, aftereffect (early post) magnitudes are shown in Figure 4.4B. Furthermore, our ANOVA assessing the rate of unlearning during post-adaptation (Figure 4.4C; average of first 150 strides of post-adaptation) showed no significant differences between groups ($F(2,23) = 0.402$, $p = 0.674$). Taken together, these results demonstrate that varying the type of perturbation did not influence the amount of motor learning or retention.

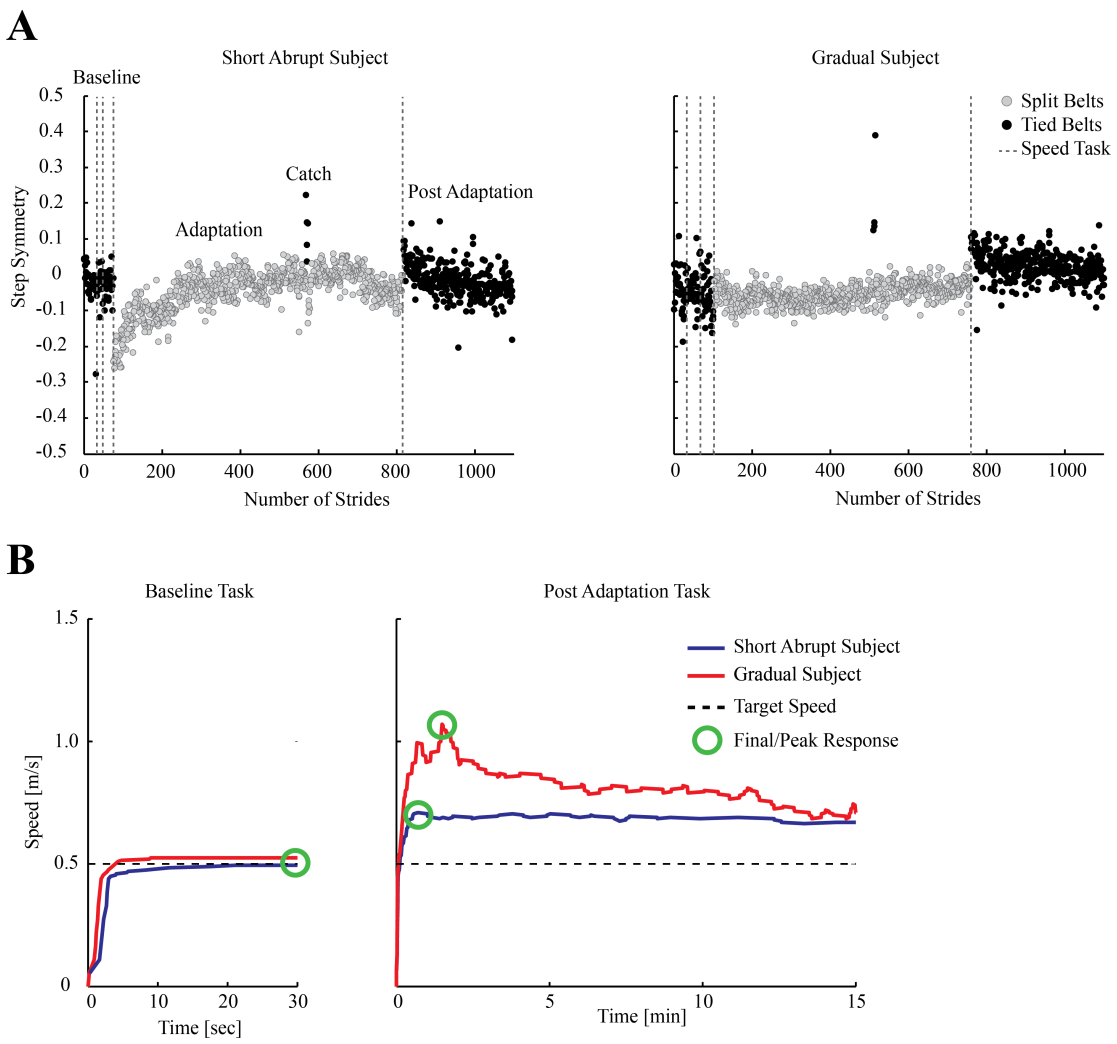

Figure 4.3 Single subject motor (step symmetry) and speed matching task responses for typical Gradual and Short Abrupt subjects. **A**: Step symmetry (error) plotted stride by stride for two typical subjects from the Short Abrupt group (left) and Gradual group (right) in Experiment 1. Black dots show strides under tied conditions and grey dots show the adaptation period where the belts are split. The Short Abrupt subject experiences large errors at the beginning of adaptation is able to correct and achieve symmetry (value of 0) at the end of adaptation. The Gradual subject is perturbed slowly and is able to maintain symmetry throughout adaptation. Note however, that the catch trial and post-adaptation initial magnitudes show similar aftereffects despite the difference in perturbation. **B**: Right treadmill belt speed responses during speed matching tasks before (left) and post-adaptation (right) for a typical Short Abrupt subject (blue) and Gradual subject (red). Single response values for the baseline periods were designated as the final speeds achieved at the end of the 30 second task. The peak magnitudes for the post-adaptation task correspond to the maximum values within the first two minutes of post-adaptation (e.g. green circles).

4.3.2 Experiment 2 – Leg Speed Perception

While different perturbation types did not influence motor adaptation results, they led to significant differences between groups in perceptual speed recalibration. Figure 4.3B shows typical pre and post-adaptation behavior for example Short Abrupt and Gradual subjects. While at baseline both subjects are able to achieve the target speed of .5 m/s, during the post-adaptation task, the Gradual subject shows a much larger response, indicating a larger change to leg speed perception. Group post-adaptation speed perception data is shown in Figure 4.5A. As anticipated, our Kruskall-Wallis H tests showed no significant differences between groups in baseline leg speed perception ($\chi^2(2) = 0.214$, $p = 0.899$). Our Wilcoxon signed-rank tests showed significant baseline to peak post-adaptation aftereffect differences ($Z = -2.521$, $p = 0.012$; all 3 groups). However, our comparison of post-adaptation peak performance revealed a significant of GROUP ($\chi^2(2) = 8.726$, $p = 0.013$). Our Mann-Whitney U test post-hoc analysis, shown in Figure 4.5B, revealed that the Gradual group had significantly higher peak speed aftereffects than the Short Abrupt group ($p = 0.005$) but not compared to the Extended Abrupt group ($p = 0.269$). We also found a trend towards significance between the Short and Extended Abrupt groups ($p = 0.059$). In other words, perturbation type had a significant influence on the amount of speed recalibration, which occurred from split-belt adaptation, with gradual adaptation leading to the greatest change in leg speed perception.

4.3.3 Experiment 2 – Motor Performance

Confirming the results of Experiment 1, analysis of the amount of motor learning in Experiment 2 demonstrated that perturbation type did not affect motor learning. Step

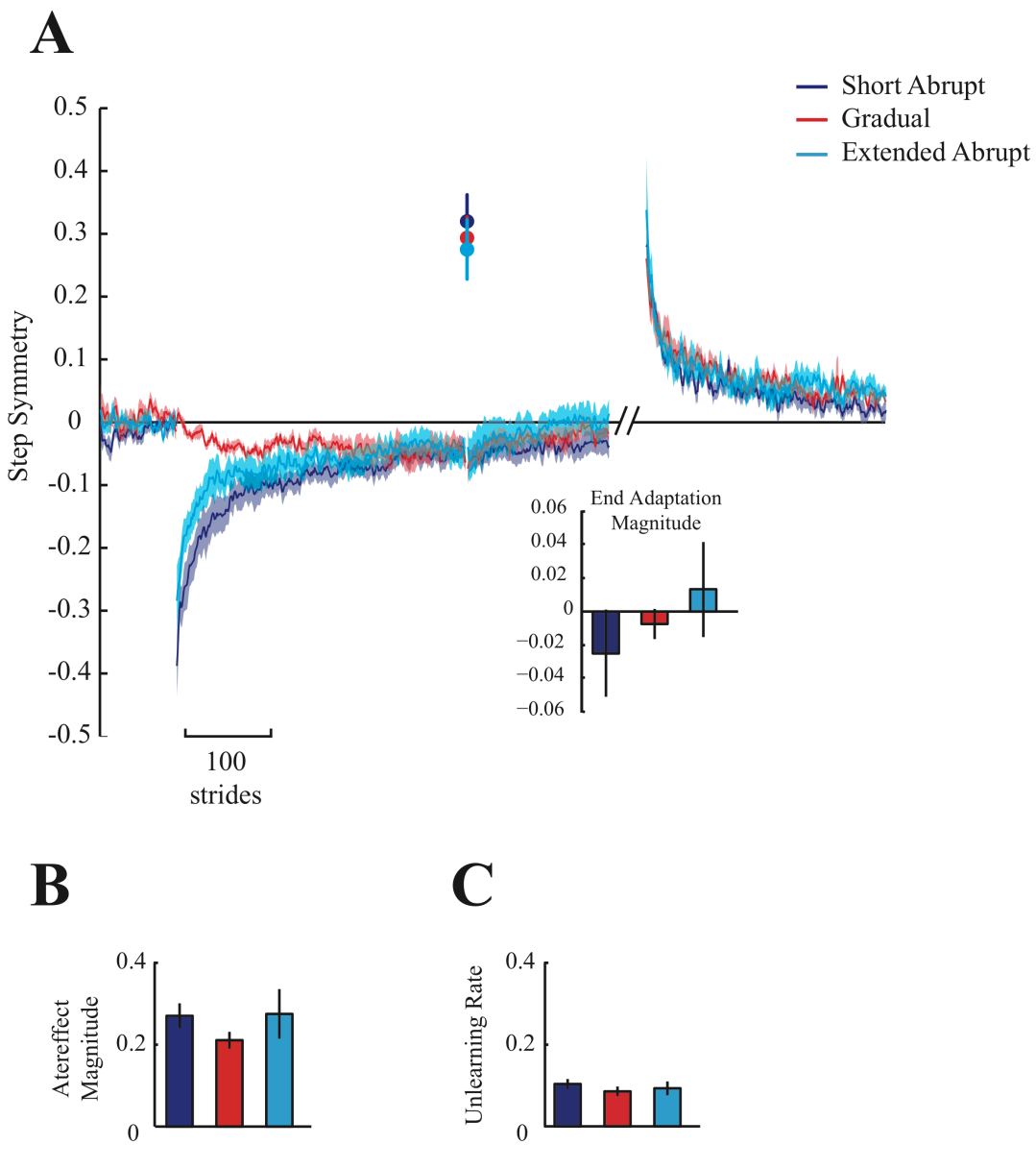

Figure 4.4 Step symmetry motor results for experiment 1. **A**: Step symmetry plotted stride by stride for the 3 groups in Experiment 1. Short Abrupt group data shown in dark blue, Gradual in red and Extended Abrupt in light blue. Data shown is smoothed with a running average bin of 3 strides and shaded area represents standard error of the mean (SEM) for each bin. Average baseline step symmetry was not statistically different between groups ($F(2,23) = 1.684$, $p = 0.21$). Average baseline values are subtracted from the curves (i.e. perfect symmetry is a value of 0). Group curves are truncated (hence the break in the graph for adaptation) in each contiguous walking block by the smallest

number of strides in each group. Inset bar graph shows group averages of step symmetry at the end of adaptation (last 30 strides). Our two-way repeated measures ANOVA of key time points showed a significant effect of TIME ($F(3,63) = 90.664$, $p < 0.001$) but no significant differences for GROUP ($F(2,21) = 0.070$, $p = 0.932$) or interaction of GROUP x TIME ($F(6,63) = 0.626$, $p = 0.616$). **B**: Step symmetry initial post-adaptation walking aftereffect averages (first 5 strides) are shown along with SEM. **C**: Post-adaptation unlearning rate averages are shown along with SEM. Rates calculated as average of the first 150 strides. No rate differences across groups were found ($F(2,23) = 0.402$, $p = 0.674$).

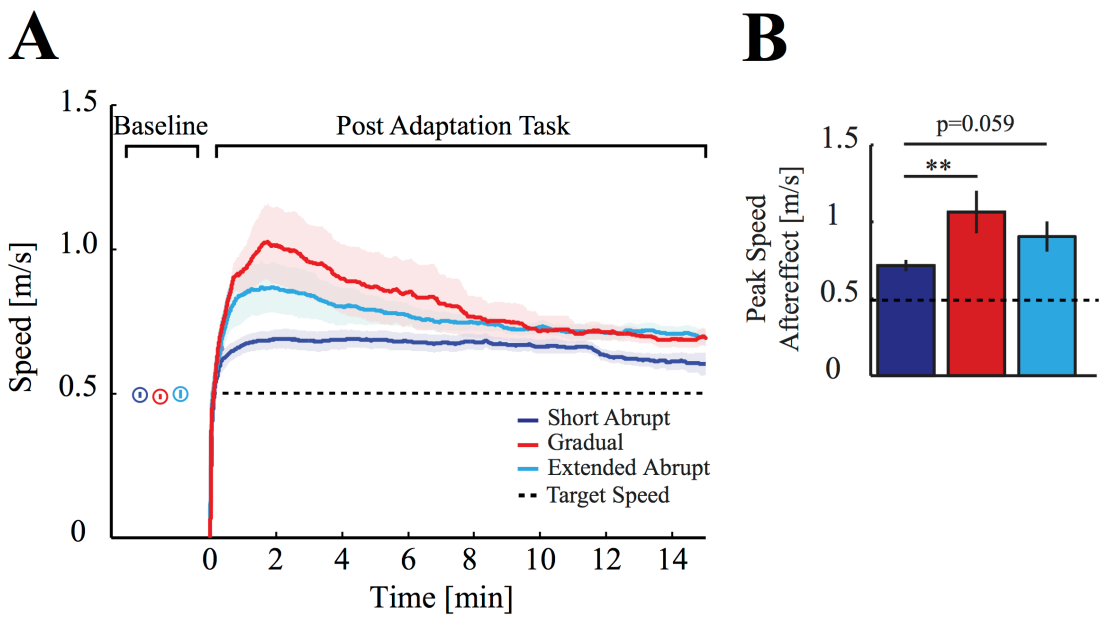

Figure 4.5 Perceptual speed task results. **A**: Right treadmill belt speed responses for baseline and post-adaptation speed matching tasks for all groups. Each subject's 3 baselines final task responses are averaged and then averaged across subjects. For post-adaptation date shown, discrete treadmill belt speed changes are up-sampled (1khz) for each subject and averaged at each time point across subjects. Error bars and shaded regions represent SEM. Anything above the target speed (dashed line) is an aftereffect that suggests the subject's right leg feels slower and they compensate by speeding it up. Kruskall-Wallis H tests showed no significant differences between groups in baseline leg speed perception ($\chi^2(2) = 0.214$, $p = 0.899$). **B**: Peak speed task aftereffect magnitude averages for all groups. Our comparison of post-adaptation peak performance revealed a significant effect of GROUP ($\chi^2(2) = 8.726$, $p = 0.013$). Mann-Whitney U test post-hoc analysis showed that the Gradual group had significantly higher peak speed aftereffects than the Short Abrupt group ($p = 0.005$) but not compared to the Extended Abrupt group ($p = 0.269$). We also found a trend towards significance between the Short and Extended Abrupt groups ($p = 0.059$).

symmetry for each group is shown in Figure 4.6. Baseline values were not found to be significantly different between groups ($F(2,23) = 2.517$ $p = 0.105$). As in Experiment 1, our two-way repeated measures ANOVA showed a significant effect of TIME (catch, late adapt, early post and late post) ($F(3,63) = 71.639$, $p < 0.001$) but no significant differences for GROUP ($F(2,21) = 0.893$, $p = 0.424$) or interaction of GROUP x TIME ($F(6,63) = 0.947$, $p = 0.424$). Furthermore, analysis of the unlearning rate in Experiment 2 also showed no significant difference between groups ($F(2,23) = 3.06$, $p = 0.068$), corroborating our results from Experiment 1 and suggesting that any motor unlearning during the 15 minute post-adaptation task was similar across subjects as well.

4.3.4 Experiment 2 – Extended abrupt group achieves adapted state during speed matching task

To determine what motor strategies subjects employed while performing the speed matching task, we quantified individual leg step lengths and step times at the end of adaptation (mean of the last 30 strides) and at the peak speed task response (mean of 5 strides at peak) (see Figure 4.7). Our ANOVA for slow step length (Figure 4.7A) revealed significant effects of TIME ($F(1,21) = 49.572$, $p < .0001$), GROUP ($F(2,21) = 7.426$, $p=0.004$), and a GROUP x TIME interaction ($F(2,21)=18.504$, $p<0.001$). Post-hoc tests found a significant difference only between the Short Abrupt and Extended Abrupt Group ($p = 0.003$). ANOVA for fast step length (Figure 4.7B) found a significant effect of TIME ($F(1,21) = 46.695$, $p < .0001$), and a GROUP x TIME interaction ($F(2,21)=12.111$, $p<0.001$) but no effect of GROUP ($F(2,21)=1.930$, $p=0.170$). Post-hoc tests did not reveal significant differences between individual groups (Short Abrupt vs Gradual ($p = 1.0$); Short Abrupt vs Extended Abrupt ($p = 0.779$); Extended Abrupt vs

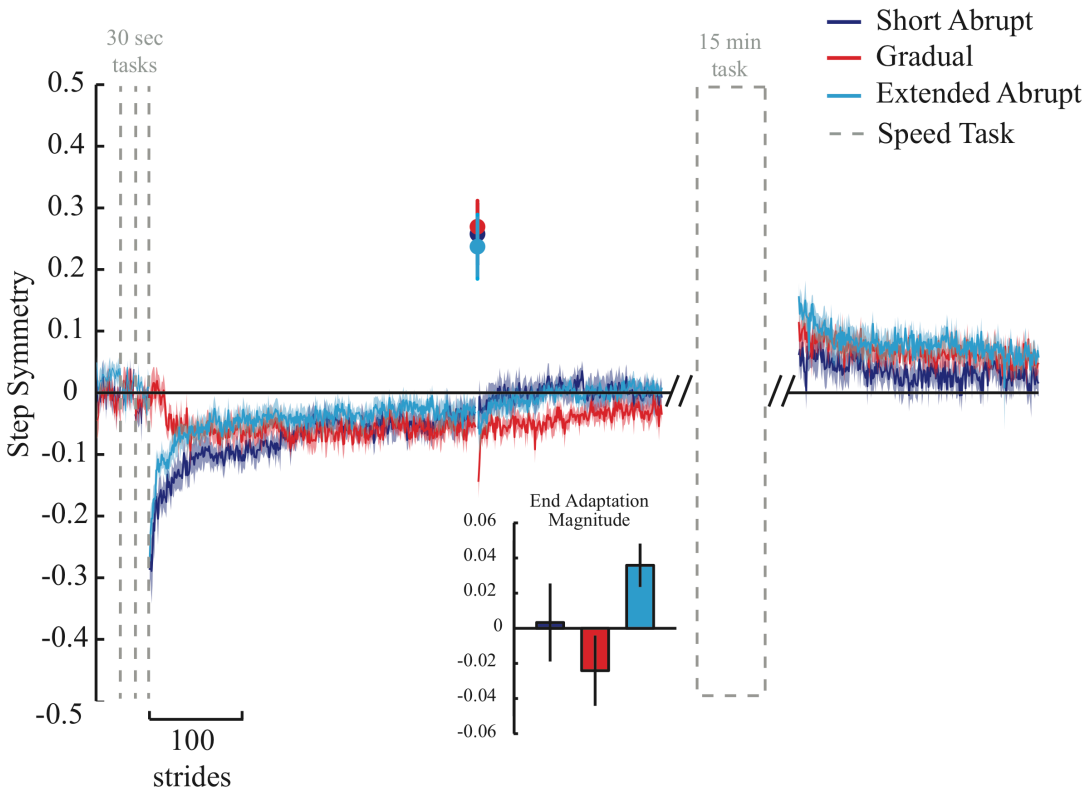

Figure 4.6 Step symmetry plotted stride by stride for all groups in Experiment 2. Group colors are consistent with Experiment 1. Data shown is smoothed with a running average bin of 3 strides, baseline average subtracted, and truncated in each contiguous walking block by the smallest number of strides in each group. Shaded areas and bars represent SEM. Inset bar graph shows end adaptation step symmetry averages (last 30 strides). The grey dashed lines represent where the speed tasks took place. Confirming our experiment 1 results, our one-way repeated measures ANOVA showed a significant effect of TIME ($F(3,63) = 71.639$, $p < 0.001$) but no significant differences for GROUP ($F(2,21) = 0.893$, $p = 0.424$) or interaction of GROUP x TIME ($F(6,63) = 0.947$, $p = 0.424$).

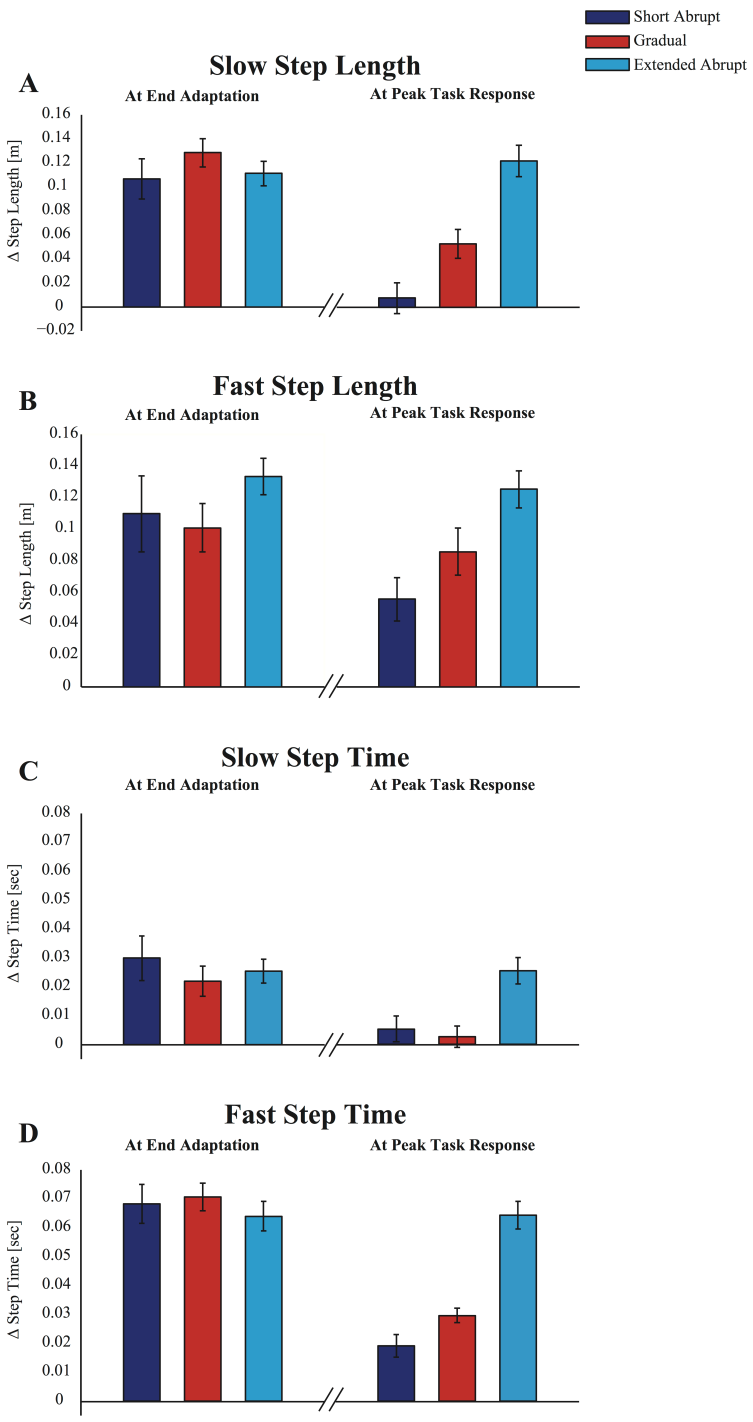

Figure 4.7 Step length and time performance during the post-adaptation speed task and at the end of adaptation. **A-B**: Slow (left leg) and fast (right leg) step lengths at the time of peak speed response (5 stride average) and at the end of adaptation (last 30 strides). Our two-way repeated measures ANOVA for slow step length revealed a significant of TIME ($F(1,21) = 49.572$, $p < .0001$) , GROUP ($F(2,21)=7.426$, $p=0.004$) and significant GROUP x TIME interaction ($F(2,21)=18.504$, $p<0.001$). Post-hoc tests showed a significant

difference only between the Short Abrupt and Extended Abrupt Group ($p = 0.003$). The Fast step length ANOVA showed a significant of TIME ($F(1,21) = 46.695$, $p < .0001$) and a significant GROUP x TIME interaction ($F(2,21)=12.111$, $p<0.001$). Post-hoc tests did not show significant differences across groups **C-D**: Our ANOVA of slow step time revealed a significant effect of TIME ($F(1,21) = 14.838$, $p =0.001$), and a significant GROUP x TIME interaction ($F(2,21)=4.614$, $p=0.02$). Post-hoc tests did not show significance for any pairwise comparisons. Our ANOVA for fast step times showed a significant of TIME ($F(1,21) = 122.489$, $p < .0001$) , GROUP ($F(2,21)=6.270$, $p=0.007$) and significant GROUP x TIME interaction ($F(2,21)=32.133$, $p<0.001$). Post-hoc analysis showed a significant difference only between the Short Abrupt and Extended Abrupt group ($p = 0.007$).

Gradual ($p = 0.193$)). Our ANOVA for slow step time (Figure 4.7C) revealed a significant effect of TIME ($F(1,21) = 14.838$, $p = 0.001$), and a GROUP x TIME interaction ($F(2,21)=4.614$, $p=0.02$), but no significant effect of GROUP ($F(2,21)=2.783$, $p=0.085$). Post-hoc tests did not show significance for any pairwise comparisons. Finally, our ANOVA for fast step times (Figure 4.7D) showed a significant effect of TIME ($F(1,21) = 122.489$, $p <.0001$), GROUP ($F(2,21)=6.270$, $p=0.007$) and a significant GROUP x TIME interaction ($F(2,21)=32.133$, $p<0.001$). Post-hoc analysis found a significant difference only between the Short Abrupt and Extended Abrupt group ($p = 0.007$). In order to support the claim that subjects were attempting to recall something about their adapted state during the post-adaptation speed task, we conducted correlations for individual groups for step lengths and times. Figure 4.8 shows the results of the Pearson correlations for step length (Figure 4.8A) and step time (Figure 4.8B). Figures show values for both fast and slow steps. The dotted reference line in these plots represents unity, which represents perfect recall of motor performance of the adapted state during peak speed task response. For step lengths, the Extended Abrupt Group showed a significant correlation between end of adaptation and peak speed task performance ($r = 0.72$, $p = 0.002$) whereas the Short Abrupt ($r = 0.49$, $p = 0.06$) and Gradual group ($r = 0.44$, $p = 0.09$) did not. For step timing, all groups showed significant correlations (Short Abrupt: $r = 0.74$, $p = 0.001$; Gradual: $r =0.94$, $p <0.001$; Extended Abrupt: $r = 0.94$, $p < 0.001$). Taken together, these results demonstrate a clear relationship between motor behavior between the end of adaptation and during the peak speed task response. Further, given the proximity of their data to the unity line, it appears

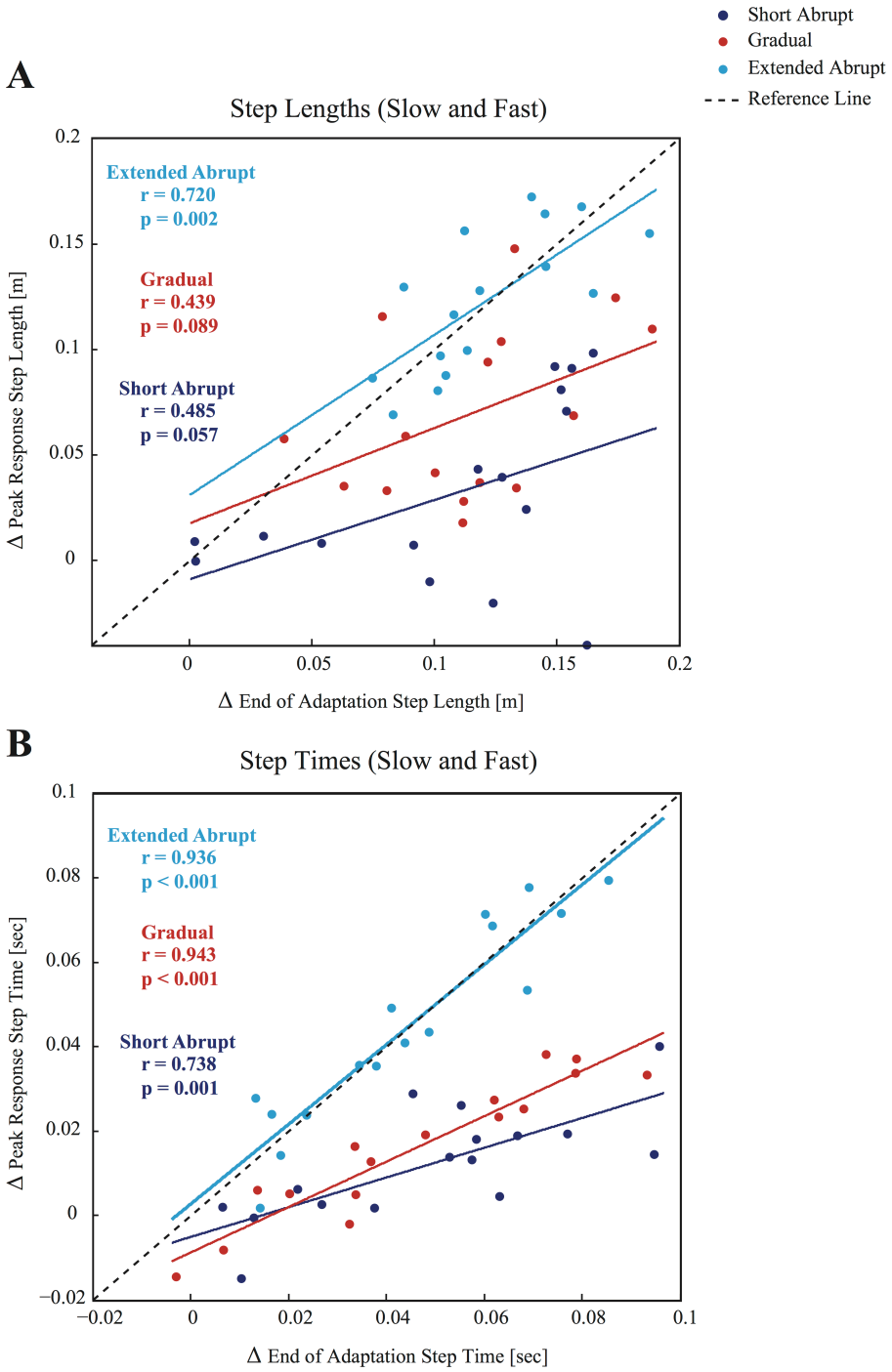

Figure 4.8 Group correlations for (baseline subtracted) motor behavior at peak post-task speed response and at end of adaptation. Linear regression fits for each group are color coded accordingly and the reference line (black dashed) shows perfect recreation of end adaptation motor performance. Slow and fast step lengths and times are pooled together for each group. **A**: Correlations for step lengths in meters shown. Pearson correlations showed a significant relationship for the Extended Abrupt Group (r = 0.720, p = 0.002)

and trending for the Short Abrupt ($r = 0.485$, $p = 0.057$) and the Gradual groups ($r = 0.439$, $p = 0.089$). **B**: Step time correlations in seconds shown. Significant Pearson correlations were found for the Extended Abrupt ($r = 0.936$, $p < 0.001$), Gradual ($r = 0.943$, $p < 0.001$) and Short Abrupt groups ($r = 0.738$, $p = 0.001$). However, the Extended Abrupt Group appeared to be the closest to the unity line (perfect recreation of end adaptation state).

that the Extended Abrupt group is more accurately recalling performance from the adapted state.

4.4 Discussion

The goal of this study was to determine whether inducing movement errors of difference sizes and doses could modulate the amount of learning in both the motor and sensory domains after split-belt treadmill walking. Our results demonstrate that gradual, abrupt, and extended abrupt perturbations lead to similar motor learning, but different amounts of sensory recalibration. Specifically, a gradual perturbation that led to small sensorimotor errors, led to the greatest recalibration of leg speed perception. Furthermore, our analysis also suggests that the mechanism by which the gradual and abrupt perturbations recalibrated perception may be different, with the gradual perturbation being more directly related to a pure change in perception.

While all groups demonstrated significant aftereffects in leg speed perception after split-belt adaptation, the largest effects were seen in the Gradual group. The changes in perception for the Gradual group in the current study appear to be larger than the analogous changes seen in felt hand position in visuomotor adaptation studies. For example, Salomonczyk and colleagues (2011) showed that after adapting to an abrupt visuomotor rotation, subjects exhibited a 7.3 degree shift in perceived hand position compared to estimates following training with an aligned cursor - a *24.3%* change relative to the magnitude of the perturbation. Similarly, a gradual perturbation resulted in a *21%* change in perceived hand position. In split-belt walking adaptation, walking speed perception seems to be more of a salient percept. If we consider our speed perturbation

to be 1 m/s (left leg = .5 m/s, right leg = 1.5 m/s), our short abrupt perturbation would result in a roughly 21% change in leg speed perception (based on an absolute change of .21 m/s). However, our gradual perturbation resulted in a roughly 51% change in perception (absolute change of .51 m/s). Larger aftereffects in the Gradual group we observed may be explained by the active/passive nature of our speed perception task. When Mattar et al. (2013) compared abrupt versus gradual learning from a force-field reaching adaptation task, they quantified the perceptual aftereffect for the Abrupt group as 15.6% of the magnitude of the change in movement curvature due to motor learning. In their perceptual task, they had subjects actively move outward in a force channel and were asked if they had been moved to the right or left of their body midline. While they did not measure the amount of motor learning for their Gradual group, as we have, it appears that their Gradual group changes twice as much as their Abrupt group, about 30% of the motor perturbation. This possibility suggests that when asked to make a perceptual sensory judgement after a motor learning task, if the judgment is made *during* active movement (as in Mattar et al., 2013; Ostry et al., 2010; and our current study) then one could perhaps induce a larger change in perception compared to a judgment made when the limb is not moving (Salomonczyk, Cressman and Henriques). Future studies will need to explicitly compare the effects of movement during perceptual judgment to elucidate this possibility.

As mentioned before, our most recent results (Patrick et al., 2014) are consistent with our current results in that Abrupt vs. Gradual split-belt learning shows similar motor aftereffects and decays. Another recent locomotor learning study that used a novel resistance to the forward advancement of one leg suggests locomotor adaptation using

gradual vs. abrupt perturbation schedules does not significantly impact retention of the adaptation 24 h after initial learning (Hussain & Morton, 2014). This is a different type of locomotor learning in that the perturbation is a direct force on the leg during swing phase but shows similar results to our current study.

In contrast to the effect on sensory recalibration, our results showed that different perturbation schedules did not influence the amount of motor adaptation. Previous studies have had contradictory findings in regards to the influence of abrupt versus gradual perturbations on motor adaptation. For instance, our current findings concur with those of Patrick et al. (2014) and Hussain and Morton (2014) who showed that gradual and abrupt perturbations did not significantly alter the magnitude (retention) of motor adaptation. On the other hand, Torres-Oviedo and Bastian (2012) found that gradual adaptation led to a smaller magnitude of motor adaptation compared with abrupt or noisy gradual adaptation. One possible explanation for this discrepancy is the manner in which the gradual perturbation was introduced. The present study utilized a paradigm described by Patrick et al. (2014), for which the treadmill began with tied belts at 0.5 m/s and one belt was gradually increased to 1.5 m/s. Torres-Oviedo and Bastian (2012), however, began the treadmill with tied belts at 1.0 m/s and simultaneously decreased the speed of one belt to 0.5 m/s and increased the other to 1.5 m/s. While the reason is not clear, it appears that such variations in the manner a gradual perturbation is applied can influence the effect of the adaptation. In the future, systematically studying the effects of introducing a perturbation in varied ways could help elucidate the true effect of different perturbation schedules on motor adaptation.

One important consideration in the effect of different perturbation types on motor adaptation is the role of cognitive strategies. Real world motor skills are traditionally taught via explicit information about how to accomplish a task. The motor adaptation literature, on the other hand, primarily focuses on implicit mechanisms of learning driven by sensory prediction errors. Recent research shows that overall task performance on a visuomotor adaptation task is composed of both an explicit aiming direction (i.e. a cognitive strategy) and an implicit learning mechanism (Taylor et al., 2014). However, most such studies have not addressed how a gradual perturbation might differentially affect the explicit vs. implicit learning mechanisms, or how they are related to perceptual changes. Our results may suggest that explicit strategies employed during abrupt split-belt adaptation may preclude subjects from fully recalibrating their sense of leg speed, yet gradual adaptation may allow for greater sensory recalibration due to less involvement of explicit mechanisms. This idea is supported by recent split-belt treadmill work (Sawers et al., 2013) where subjected simultaneously adapted to either an abrupt or gradual perturbation and measured reaction times in a cognitive task. While motor performance was similar between groups, their cognitive task results showed increased reaction times at the beginning of the adaptation period for the group that adapted abruptly. This suggests there may be shared cognitive resources that are specific to an abrupt split-belt perturbation and as previously stated, might conflict with recalibration of leg speed perception.

Our perceptual aftereffect results for the Extended Abrupt group revealed a trend towards significance compared to the Short Abrupt group ($p = 0.059$). Though our motor results did show a difference in retention, this is consistent with our initial hypothesis that

longer adaptation would allow for larger perceptual recalibration. Perhaps if we would have extended the amount of adaptation to an even longer period, it is possible that we would have observed results closer to the gradual aftereffects. Interestingly, our post-hoc analysis of the motor performance during the post-adaptation task showed that the Extended Abrupt group was attempting to achieve their adapted state more so than the other groups, despite the Gradual group showing larger perceptual aftereffects. This suggests that the Extended Abrupt group's change in perception seemed to be more linked to a reinforced motor state while the Gradual group's recalibration might be due to a separate implicit component affecting perception preferentially. Joiner and Smith (2008) found this to be the case in the *motor* domain for a force-field reaching study where they found that overlearning resulted in more retention 24 hours after learning. They argue that the level of performance achieved by subjects was not as important for retention but rather the level of a specific component process in a multi-rate model of short-term memory formation. It is possible that in locomotor adaptation this "slow process" that responds slowly to error but retains information well is more relevant to perceptual than motor recalibration. The mechanism by which gradual and extended abrupt perturbations affect perceptual recalibration needs to be studied further. Also it would be interesting to study retention of these perceptual changes across days.

Though the evidence is still unclear, recent work has begun to discover the potential brain areas and neural circuits that are important for perceptual sensory changes that may accompany motor learning in reaching. The cerebellum has been the most studied in this work, as we know it has been shown to be important for various types of motor adaptation paradigms (Baizer et al., 1999; Burciu et al., 2014; Criscimagna-

Hemminger et al., 2010; Donchin et al., 2012; Fernandez-Ruiz et al., 2007; Martin et al., 1996a, 1996b; Maschke et al., 2004; Morton & Bastian, 2006; Rabe et al., 2009; Smith & Shadmehr, 2005; Taig et al., 2012; Werner et al., 2010, 2009). However, the relationship between the cerebellum's role in abrupt versus gradual perturbations, and motor and perceptual sensory aftereffects is still unclear. First of all, some reaching studies have argued that patients with cerebellar damage can indeed learn and show motor aftereffects given a gradual but not abrupt perturbation (Criscimagna-Hemminger et al., 2010; Henriques et al., 2014; Izawa et al., 2012). Others argue that patients and controls show similar aftereffects with both perturbation types (Gibo et al., 2013; Schlerf et al., 2013). If motor recalibration drives perceptual changes, as other studies have suggested (Mattar et al., 2013; Ostry et al., 2010), then it would be possible for a damaged cerebellum to recalibrate sensory perception give an appropriate (gradual) perturbation. Indeed, a recent reaching study showed that cerebellar patients showed similar motor and perceptual aftereffects to that of controls (Henriques et al., 2014). The authors argue that the cerebellum is not needed for this type of perceptual recalibration but it is likely that the result would be different given an abrupt perturbation. In walking adaptation, it has not been studied how abrupt versus gradual perturbations, in cerebellar patients, preferentially affect motor and/or perceptual aftereffects. This would be important to investigate and extend the currently unclear reaching adaptation literature.

We have shown that learning a new walking pattern through different perturbation schedules results in different amounts of recalibration of the sense of leg speed during walking, but does not affect the amount of motor recalibration. Specifically, adapting to a gradual split-belt treadmill perturbation induced the largest sensory aftereffects compared

to abrupt or extended abrupt adaptation. We speculate that the persistence of small errors during gradual adaptation increases the likelihood of errors being attributed to internal factors, thus reducing the explicit contributions to adaptation and facilitating greater sensory recalibration. While we believe the cerebellum plays an important role in this type of sensorimotor adaptation, it has yet to be determined which neural mechanisms may underlie the effect of gradual vs. abrupt adaptation on sensory recalibration. Future studies investigating these neural mechanisms will further understand the link between sensory and motor adaptation.

CHAPTER 5

Implications and Future Directions

This dissertation investigated the perceptual sensory correlates of split-belt locomotor adaptation, their relationship to motor learning and the involvement of the cerebellum in these forms of sensorimotor recalibration. Our results add to the limited literature on lower limb perceptual changes that accompany motor learning and demonstrate some differences to current analogous reaching studies. We have also explored perceptual sensory recalibration modalities (speed and force) that have not been explored in the current reaching literature. We have developed a speed perception paradigm that both healthy individuals and cerebellar ataxia patients can perform, though only health individuals show post-adaptation aftereffects. Along these lines, this paradigm could be used in the future, along with other standard exams, to provide further evidence of potential damage of the cerebellum.

What are the perceptual sensory correlates of split-belt adaptation? Numerous studies have investigated the phenomenon of a change in perceived hand position following reaching adaptation paradigms (Cressman & Henriques, 2009, 2010; Haith et al., 2008; Mattar et al., 2013; Ostry et al., 2010; Salomonczyk et al., 2011, 2012). In attempting to expand on this literature, but for the lower limbs, we found that perceived foot position or stepping force did not change significantly, while speed perception changed robustly following split-belt walking adaptation. These results are consistent with an earlier study (Jensen et al., 1998) and additionally we were able to quantify the

time decay of aftereffects and the relationship to motor change. Furthermore, our control group results, which had not been previously tested, showed that fast tied-belt walking did not recalibrate speed perception, maintaining that this recalibration is an error-driven process. We were also able to confirm previous results (Choi & Bastian, 2007) that indicate there are independent control networks for walking and extend this to also include changes in speed perception. These results suggests that speed is a salient perception in learning a new split-belt walking pattern and this knowledge may be leveraged for different types of learning paradigms such as reinforcement learning where feedback of a subject's leg speed may expedite learning. Other important future work may include 1) investigating how generalizable this perceptual recalibration is at different speeds and 2) testing whether similar perceptual changes occur if the speed task is conducted passively such that the treadmill moves the subject's legs and a two-alternative forced choice task is done. In the following studies, we aimed to investigate how cerebellar damage affects this phenomenon and also how we could modulate it by altering the learning environment.

Does damage to the cerebellum result in motor and speed perception recalibration deficits? Classically, it has been shown that individuals with cerebellar damage or degeneration have difficulties with motor adaptation (e.g. Manto et al., 1994; Maschke et al., 2004; Morton & Bastian, 2006; Smith & Shadmehr, 2005). More recently, studies in the reaching literature have begun to explore cerebellar patient recalibration deficits in felt hand position and movement (Henriques et al., 2014; Izawa et al., 2012; Synofzik et al., 2008). Building on this body of work and using our robust paradigm developed in Chapter 2, we aimed to understand the relationship between motor deficits and potential

perceptual deficits. First of all, our results are the first to show a clear preservation of learning in a temporal parameter of walking in cerebellar ataxia patients, though we have implicated this in prior work (Jayaram et al., 2012; Patrick et al., 2014; Vasudevan et al., 2011). Furthermore, we found that deficits in a spatial motor parameter were linked to deficits in recalibration of leg speed perception. Through this analysis we were able to get a better understanding of how it is that subjects were achieving perceptual symmetry, expanding on our work from Chapter 2. As mentioned before, the clear evidence for perceptual deficits in cerebellar patients points to a potential clinical implication of using this speed perception and motor learning paradigm to provide more evidence for potential cerebellar dysfunction in a patient. In the future, it will be important to understand what other types of learning mechanisms cerebellar patients use that contribute to motor and perceptual recalibration. For example, recent evidence (Caliandro et al., 2015) has shown an increase in prefrontal cortex activity that is linked to compensatory gait mechanisms in patients with cerebellar ataxia. This suggests ataxia patients may be using a cognitive strategy during walking. It would be of interest for future work to investigate the role of the prefrontal cortex in cerebellar patients during motor and perceptual recalibration on the split-belt treadmill by potentially modulating excitability using non-invasive brain stimulation. Future work should also be focused on examining other patient populations, for example patients with cerebral strokes, to understand how different parts of the brain such as motor cortex and parietal cortex contribute to the perceptual phenomenon we have shown.

How are motor and speed perception aftereffects modulated when the learning environment is changed? In Chapter 4, we showed that when healthy subjects learned

from different size errors and doses on the split-belt treadmill, they exhibited drastically different perceptual aftereffects despite showing similar extents and amounts of motor learning. This was surprising to find considering there is reaching adaptation studies that show that gradual perturbations (Kagerer et al., 1997; Klassen et al., 2005) as well as extended practice (Melnick, 1971; Melnick et al., 1972; Schendel & Hagman, 1982, 1991) can lead to more motor retention than abrupt perturbations. Our initial hypothesis that smaller errors might be more attributable to self-generated errors and consequently result in larger perceptual aftereffects was verified. However, we are still unsure about the mechanism by which this occurs. What we do understand from our post-hoc analysis is that our extended abrupt (overlearning) group attempted to recreate their adapted state, more so than the other groups, during the initial post-adaptation task. This suggests that the mechanism responsible for recalibrating perception in the Gradual group was much more related to a change in perception rather than a change in motor behavior with perceptual aftereffects as a byproduct. What's interesting and puzzling about these results is that one would expect that in a perceptual task that is directly related to voluntary/active movement, the amount of perceptual change should be related to the amount of learning in the motor domain but clearly was not. This suggests that while these recalibrations occur concurrently they may be independent or only partially linked. Future work should be targeted at understanding the mechanism by which gradual adaptation produces larger perceptual aftereffects. Studies in reaching adaptation should carry out these explicit comparisons of perturbation type on perception. Also, as Mattar and colleagues (2013) have done in force-field reaching adaptation it would be helpful to conduct a study that probes speed perception throughout adaptation as we have only

carried out the speed matching task proceeding the adaptation period.

In summary, we have shown that the healthy nervous system proves it to be beneficial to recalibrate speed perception after experiencing different types of novel split-belt errors. This potentially allows for the optimization of limb kinesthetic estimation, though the mechanism is unclear at this point. This dissertation highlights the importance of sensory perception and its relationship to motor learning. Future work will likely elucidate this relationship and will perhaps be able to leverage it to do "perceptual training" in order to affect motor learning, which has potential clinical implications. Finally, our results in cerebellar ataxia patients show the first piece of evidence that suggests they may not be deficient in learning of temporal parameters of walking. This underlines the importance of dividing behavioral analysis of patient populations into separate parts, to understand what aspects of their behavior is deficient and the implications for the corresponding neural mechanisms. Once we gain a better understanding of motor/perceptual recalibration mechanisms we may be able to use mobile solutions such as smart phones and devices like the Xbox Kinect or Google Glass to provide real-time feedback in order to strengthen learning for patient populations in the real world.

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Curriculum Vitae

Alejandro Vazquez was born on January 29, 1986 in Torreon, Coahuila, Mexico. He migrated to the United States at the age of two. He graduated as Valedictorian of Henry J. Kaiser High School in Fontana, CA in 2004. He received a Harbison Scholarship to attend the Massachusetts Institute of Technology. In 2008, he graduated from MIT with a bachelor's degree in Electrical Engineering and Computer Science. While at MIT, he conducted research in the Department of Architecture, the Media Lab and completed his undergraduate thesis with Dr. George Church at Harvard Medical School. He also held two industry internships with IBM in the summers of 2006 and 2008. In 2008, Alejandro began the Biomedical Engineering PhD program at Johns Hopkins University, and joined the Motion Analysis Laboratory in the Kennedy Krieger Institute. Dr. Amy Bastian mentored him throughout his doctoral research. As part of the PhD program, he was a teaching assistant for a yearlong biomedical engineering undergraduate design course and also spent a year as co-president of the PhD Council. His research focuses on the motor and sensory perceptual changes that occur while learning new walking patterns in healthy and cerebellar ataxia patients.